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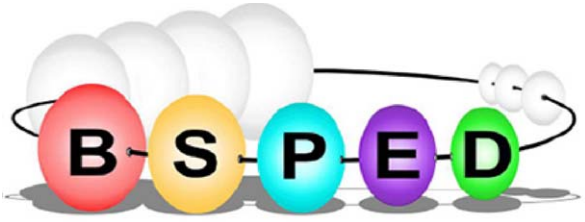

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Abstract Unavailable

DOI: 10.1530/endoabs.85.CME1.1

CME1.2

Abstract Unavailable

DOI: 10.1530/endoabs.85.CME1.2

CME Symposium 2

CME2.1

An approach to hypo/hypercalcemia

Raja Padidela
Royal Manchester Children's Hospital, Manchester, United Kingdom

Calcium (Ca) is critical for a multitude of biological processes in the human body. Ca concentration is therefore tightly controlled in all age groups between 2.2-2.7 mmol/l. When Ca intake is low, extracellular fluid Ca can potentially decrease. The parathyroid cell is exquisitely sensitive to minor alterations in Ca level and a rise in PTH normalises the reduced serum Ca concentration because of its action on (1) the intestine, by increasing Ca absorption, indirectly by its effects on calcitriol (1,25(OH)2D) production, (2) the bone, by increasing Ca efflux from the bone and (3) the kidneys, by increasing Ca reabsorption and excreting inorganic phosphorus. Hypocalcemia can occur at any age; it may arise because of inadequate calcium supply (reduced dietary intake or vitamin D deficiency or defects in its metabolism), following an acute increase in plasma phosphate concentration, impaired parathyroid hormone (PTH) secretion and end-organ resistance to PTH (e.g., pseudohypoparathyroidism). Hypomagnesemia impairs PTH secretion and leads to resistance to the action of PTH on the bone and kidney. Hypercalcemia develops when the rate of calcium entry into the extracellular fluid exceeds the kidneys' capacity for its excretion. It occurs when there is increased absorption of calcium from the gastrointestinal tract, increased release of calcium from the skeleton or decreased excretion of calcium from the kidneys. Symptoms of hypercalcemia in infants are often non-specific and include feeding difficulties, vomiting, constipation, failure to thrive, irritability and hypotonia. Older children may present with anorexia, non-specific abdominal pain, muscle weakness, polydipsia and polyuria, dehydration, and neuropsychiatric symptoms. Chronic hypercalcemia and accompanying hypercalciuria may predispose to nephrocalcinosis and, if left untreated, renal impairment. In this presentation, I will discuss my approach to the investigation and management of hypo and hypercalcaemia using some of the cases I have managed in my practice.

DOI: 10.1530/endoabs.85.CME2.1

CME2.2

Abstract Unavailable

DOI: 10.1530/endoabs.85.CME2.2

CME Symposium 3

CME3.1

Genetic approach to Short stature

Helen Storr
Professor of Paediatric Endocrinology, Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University London, London, United Kingdom

Children referred to paediatric endocrinology clinics have variable degrees of short stature and growth failure. There is a wide range of potential aetiologies ranging from normality to an abnormal growth pattern which will lead to adult height below the target height range. Early investigation and diagnosis of short stature is important to prevent delays in the access to appropriate therapies which will improve final height. Genetic variants impacting cellular pathways, hormones and growth factors can result in short stature and a significant proportion of short patients presenting to clinic remain undiagnosed despite extensive investigation. Genetic testing of children with short stature has led to the identification of new causes of short stature, clarified the physiology of human growth and can indicate the correct therapeutic approach. The investigation of short stature patients should combine clinical assessment, endocrine evaluation and genetic sequencing. It is important for clinicians to understand the genetic tools available and their interpretation.

DOI: 10.1530/endoabs.85.CME3.1

CME3.2

Neonatal diabetes

Sarah Flanagan
University of Exeter, Exeter, United Kingdom

In recent years there has been significant progress in defining the genetic aetiology of neonatal diabetes with disease-causing variants identified in over 30 genes. These genes are all recognised as having a critical role in the development, function, or destruction of the pancreatic beta-cell. Targeted next generation sequencing allows for the rapid, simultaneous screening of all 30 known neonatal diabetes genes. This analysis provides an accurate genetic diagnosis for over 80% of individuals which is important as identifying the genetic subtype will inform on whether an individual will have isolated diabetes or syndromic disease where diabetes is often the presenting feature. A genetic diagnosis will also provide accurate information on recurrence risk within families, and crucially it will inform on treatment decisions leading to improved clinical outcome. A small minority of individuals without a disease-causing variant in a known neonatal diabetes gene have extreme early-onset type 1 diabetes as shown by the presence of autoantibodies in combination with a high polygenic risk score. For the remaining individuals with genetically unsolved disease, there is strong evidence from phenotyping studies and Mendelian inheritance patterns within families to support there being undiscovered genes for neonatal diabetes. Next generation sequencing technologies also provide exciting possibilities for large scale sequencing studies with whole genome sequencing allowing for a gene agnostic approach to genetic discovery. Continuing to discover new genes for neonatal diabetes is important as it will provide further insights into pancreatic beta-cell biology as well as the pathways of autoimmunity which will be important for type 1 diabetes research.

DOI: 10.1530/endoabs.85.CME3.2

CME Symposium 4

CME4.1

Abstract Unavailable

DOI: 10.1530/endoabs.85.CME4.1

Endocrine Main Meeting Sessions

Endocrine Symposium 1

EMM1.1

Congenital imprinting disorders

Claire Power, Sally Ann Lynch, Brónagh Ó hIcí & Susan M O' Connell
Children's Health Ireland, Dublin, Ireland

Congenital imprinting disorders (IDs) are a group of rare conditions affecting growth, metabolism and development caused by aberrant expression of imprinted genes in a parent-of-origin dependent manner. The internationally recognised IDs are Prader Willi Syndrome (PWS), Angelman Syndrome (AS), Beckwith Wiedemann Syndrome (BWS), Silver Russell Syndrome (SRS), Temple Syndrome (TS14), Pseudohypoparathyroidism (PHP), Transient Neonatal Diabetes Mellitus (TNDM) and Kagami-Ogata Syndrome (KOS14). Given their broad clinical overlap and complex underlying molecular mechanisms, diagnosis can be challenging. Mechanisms causing IDs include methylation defects, uniparental disomy, chromosomal imbalances and mutations in imprinted genes. Such mechanisms can be associated with factors such as assisted reproductive technology and advanced maternal age and it is postulated that frequency of IDs is increasing. Few population studies have been performed worldwide and for the less common IDs, frequency is unknown. We examine incidence, prevalence, genotype and clinical characteristics of IDs in Irish children. 4 years of prospective case ascertainment via the Irish Paediatric Surveillance Unit identified 47 new cases of IDs yielding an incidence of 0.9 per 100,000 in Irish children. To date, almost 200 prevalent cases have been identified via review of genetic laboratory records, paediatrician reporting and database searches at Children's Health Ireland. PWS accounts for more than one third of these while TNDM, PHP, TS and KOS are very rare. Genotype and clinical characteristics were examined through review of genetic records, parent questionnaires and retrospective chart review. $>90\%$ cases of PWS and BWS had genetic testing in the first 6 months of life reflecting high levels of recognition. Children with SRS and AS were older at time of molecular diagnosis. Rates of delivery by caesarean section, prematurity, low birth weight and admission to the neonatal unit are higher than the national averages in this cohort. The number of health professionals who have been involved in care ranged from 2 to >15. Studying the epidemiology of these conditions and their associated burden of medical care is imperative to the planning and delivery of health services to these patients.

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EMM1.2

Abstract Unavailable

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Endocrine Symposium 2

EMM2.1

BSPED consensus guidelines: emergency and peri-operative management of adrenal insufficiency in children and young people

Talat Mushtaq[1] & Hoong-Wei Gan[2]
[1]Leeds Children's Hospital, Leeds, United Kingdom; [2]Great Ormond Street Hospital for Children, London, United Kingdom

Adrenal insufficiency (AI) is characterised by a lack of cortisol production from the adrenal glands. This can be a primary adrenal disorder or secondary to adrenocorticotropic hormone (ACTH) deficiency or suppression from exogenous glucocorticoids. Symptoms of AI in children may initially be non-specific and include growth faltering, lethargy, poor feeding, abdominal pain, vomiting and prolonged recovery from infections. AI is treated with replacement doses of hydrocortisone, which, at times of physiological stress such as illness, trauma or surgery needs to be increased to avoid adrenal crises and death. Currently there are no unified guidelines for AI in those <18 years old in the UK; this can lead to a substantial variation in the management of AI in both emergency and peri-operative situations. In 2021 the Paediatric AI Group was set up under the auspices of the British Society of Paediatric Endocrinology & Diabetes (BSPED) in an effort to standardise the management of paediatric AI across the UK and NI. The group consisted of 16 individuals from 10 UK tertiary endocrine units with further input from the BSPED clinical and executive committees as well as stakeholder engagement. The management principles were used to create documents on sick day glucocorticoid recommendations, peri-operative advice, and a new BSPED emergency card; all linked and accessible from a dedicated page on the BSPED website. This standardisation of management and ready access to information should allow prevention as well as timely recognition and treatment of AI and adrenal crises in children.

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EMM2.2

Abstract Unavailable

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Diabetes Professionals Day Sessions

Diabetes and COVID Symposium

DPD1.1

Diabetes and covid symposium: introduction and the south east thames study

TonyHulse
Evelina London Childrens Hospital, London, United Kingdom

Very early in the Covid-19 pandemic it became clear that diabetes was a highly significant comorbidity with an increased risk of mortality in adults of up to 3.5 fold. At the same time, anecdotes started to circulate of an apparent unseasonal increase in incidence and severity of DKA in children and young people presenting with type 1 diabetes [T1DM]. In order to examine this further, the characteristics of children presenting with T1DM from January to July 2020 in North East and South London and the South East Paediatric Diabetes network, data being received on 178 newly diagnosed children presenting to 12 PDUs. Detailed data was also obtained on 150 children presenting in the same time period in 2019, a pre-pandemic year and also prevalence data from 2016 onwards. There was a statistically significant increase in the number of children presenting with DKA during 2020 compared with 2019 and in the severity of the DKA but this was not seen in all PDUs. Compared with the previous 4 years, 2020 was generally a high-prevalence year. Two children with severe DKA and shock were positive on SARS-CoV-2 on nasopharyngeal swabs. The short period of T1DM symptoms in children with new onset diabetes presenting in DKA in the COVID pandemic did not suggest that delay in diagnosis was the sole contributor for decompensation. This small multicentre study supported the anecdotal evidence of a link between SARS-CoV-2 and newly presenting T1DM but indicated the need for a much larger study from a wider geographical area. Thus the DIMPLES Study was launched looking at children presenting with new onset and pre-existing diabetes to EDs using the PERUKI Network. The results from DIMPLES will be presented separately in this symposium

DOI: 10.1530/endoabs.85.DPD1.1

DPD1.2

Paediatric diabetes and SARS-CoV-2 - a riddle wrapped in a mystery inside an enigma

Caroline Ponmani[1] & Michael Barrett[2,3]
[1]Department of Paediatric Emergency Medicine, Barking Havering and Redbridge University Trust, London, United Kingdom; [2]Department of Paediatric Emergency Medicine, Children's Health Ireland, Dublin, Ireland; [3]Women's and Children's Health, School of Medicine, University College Dublin, Ireland, Dublin, Ireland

Background
Paediatric emergency departments saw an unusual increased incidence and severity of DKA in children with new onset diabetes in the COVID pandemic. The DIMPLES study (Diabetes Mellitus in children and young people presenting to the Emergency Department during the SARS-CoV-2 pandemic) explored this using retrospective multicentre data from 49 EDs, providing a unique perspective of paediatric diabetes from the frontline.
Methods
We compared the characteristics of 2637 children (2746 attendances) aged 6 months-16 years presenting to EDs across UK and Ireland with new onset and pre-existing diabetes. Two distinct time periods of interest were chosen-March 1, 2020 to February 28, 2021, pandemic period, and March 1, 2019 to February 28, 2020, pre-pandemic period.
Results
There were increases in new onset diabetes (1,015 to 1,183; 17%), the vast majority of which were Type 1 diabetes. There were also increases in children presenting with DKA (395 to 566; 43%), severe DKA (141 to 252; 79%), and admissions to intensive care (38 to 72; 89%). There was a 31% reduction in children with pre-existing diabetes presenting with DKA. Time to presentation for children presenting with new onset diabetes and DKA were similar across both years. Healthcare seeking delay did not appear to be the sole contributing factor to DKA severity during the pandemic. There were no significant demographic differences in children between the two study years. The normal seasonal pattern of new onset Type 1 diabetes cases (winter peak with summer trough) was disrupted in the COVID pandemic year. 16/1028 children tested positive for SARS-CoV-2 on nasopharyngeal swabs, 13 presented with DKA. 37 children were tested for SARS-CoV-2 antibodies, eight were positive.
Conclusions
The DIMPLES study showed an increase in the number and severity of children presenting with new onset diabetes and DKA in the pandemic. Proving association or causation was challenging given the small number of children tested for COVID-19 antibodies. The causes of paediatric diabetes are complex however given the high incidence of new onset diabetes and the severity of DKA it is possible that SARS-CoV-2 may have a role as a precipitator or accelerator in a genetically predisposed child.

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DPD1.3

Abstract Unavailable

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DPD1.4

'Proving causation?': antibody studies in covid related diabetes

Rachel Beckett & Caroline Stewart
Antrim Area Hospital, Antrim, United Kingdom

Background
Population data has shown an increased incidence in Type 1 Diabetes Mellitus (T1DM) following pandemic influenza A (H1N1). Worldwide studies have shown an increase in the incidence of T1DM in 2020 and 2021. Both locally and regionally in Northern Ireland we noticed a similar increase and decided to investigate further.
Method
From March 2021 we tested newly diagnosed T1DM patients in Antrim Area Hospital for Anti-SARS-CoV-2 antibodies. If antibodies were not tested at diagnosis, we consulted their Electronic Care Record (ECR) for a positive Covid PCR test prior to diagnosis.
Results
In 2019, 40 patients were diagnosed with T1DM, 43 in 2020, 41 in 2021 and as of 14/09/22 there have been 23 diagnosed in 2022. In 2021, 30/41 patients had antibodies tested, and 6 were positive. No patients who did not have antibodies tested had a positive PCR result and 2 patients had positive PCR at diagnosis but negative antibodies (8/41 (19.5%) had evidence of Covid infection) To date in 2022, 23 patients have been diagnosed with Type 1 Diabetes. 13/15 have tested positive for antibodies, 4 had a positive PCR test prior to diagnosis but were not tested for antibodies. There is evidence of Covid infection in 17/23 (74%) patients.
Discussion
Our 74% infection rate in patients with T1DM is much higher than the general population, which is 37.4% in the 0-14 years age group, based on positive PCR tests. However, the Office for National Statistics estimated that in March 2022; 82% of primary and 99.3% of secondary school age children in England had detectable Covid antibodies, therefore our figures may reflect true levels in the population as PCR testing can be influenced by health seeking behaviour as evidenced by the fact that only 4/19 (21%) with a positive antibody test had a positive PCR result.

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DPD1.5

Abstract Unavailable

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DPD1.6

Abstract Unavailable

DOI: 10.1530/endoabs.85.DPD1.6

Diabetes Symposium 2

DPD2.1

The Impact of diabetic ketoacidosis on glycaemic control

Edna Roche
The University of Dublin, Trinity College Dublin, Dublin, Ireland. CHI at Tallaght University Hospital, Dublin, Ireland

Children and young people (CYP) at clinical onset of Type 1 diabetes (T1D) usually present with the classical symptoms of polyuria, polydipsia and weight loss with evidence of hyperglycaemia. A proportion with new onset T1D progress to metabolic decompensation and present with diabetic ketoacidosis (DKA), characterised by hyperglycemia and acidosis. DKA is a major medical emergency which untreated results in coma and death. The proportion of those with DKA at diabetes onset varies widely in different populations, with many developed countries, including Ireland, reporting extremely high rates of 40%. DKA is potentially fatal, primarily due to cerebral oedema. Up to 35% of those who survive cerebral oedema have ongoing morbidity. Those who experience DKA at diabetes diagnosis have evidence of morphological and functional brain changes. Even uncomplicated DKA is associated with lower cognitive function. Poor glycaemic control at diabetes diagnosis is associated with increased diabetes related complications in young adults and increased mortality evident even 27 years later. Poor metabolic control at diagnosis establishes a trajectory of poor control evident many years later. The severity of DKA at diagnosis impacts glycaemic control up to 15 years later where those with severe DKA at diagnosis have an HbA1c which tracks 1.4% higher than those without DKA. DKA at diabetes diagnosis is considered a modifiable factor with earlier presentation to clinical services preventing the development of DKA in the majority. Increased awareness of the symptoms of T1D among the medical community and general population is thought to promote earlier presentation to clinical services and prevent DKA at diagnosis. The first health promotion campaign in Italy, the Parma campaign had a dramatic impact reducing DKA from 78% to 12.5%. The "TEST" campaign is underway to target the very high DKA rate in Ireland. Preventing DKA at diabetes diagnosis is a key therapeutic target.

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DPD2.2

Abstract Unavailable

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Diabetes Symposium 3

DPD3.1

Abstract Unavailable

DOI: 10.1530/endoabs.85.DPD3.1

DPD3.2

Abstract Unavailable

DOI: 10.1530/endoabs.85.DPD3.2

Personal Practice Session

DPD4.1

Abstract Unavailable

DOI: 10.1530/endoabs.85.DPD4.1

DPD4.2

CHOICE - structured diabetes education programme for children and young people in northern ireland

Andrea McDougall & Jacqueline McVeigh
Royal Belfast Hospital for Sick Children, Belfast, United Kingdom

It is widely recognised that diabetes education allows for improved time in range and glycaemic control, hopefully leading to improved health outcomes and therefore quality of life of those living with Type 1 diabetes. The school of nursing team at University of Ulster led by David Chaney, identified a lack of structured diabetes education for children and young people with Type 1 Diabetes in Northern Ireland. A multi-centred Randomised Controlled Trial (RCT) was designed which involved 135 adolescents across seven hospital sites in Northern Ireland, targeting 13-19 year olds. Half of the adolescents received a structured diabetes education programme named CHOICE, and the Control group received their usual routine diabetes care. Results from the RCT Coates *et al* (1), showed with delivery of CHOICE, there was no significant difference in HBA1c despite a more flexible diet at 12 months however there was an improved HBA1c at 24 months (% (mmol/mol) 9.53(81) v 8.99(75). (1) Following this RCT, CHOICE was offered during the period 2009 – 2015, to all young people up to the age of 19 with a diagnosis of Type 1 Diabetes in both the North and South of Ireland. This work was successfully funded via a Cross Border Diabetes Project named Co-Operation and Working Together (CAWT). CHOICE continues to be delivered 7 years on within each of the 5 health care trusts in the North of Ireland by a Paediatric Diabetes Specialist Nurse and a Paediatric Diabetes Specialist Dietitian. CHOICE participation involves 12 hours of interactive learning delivered in groups or as one to one, over four consecutive weeks in 3 hourly sessions. Families are encouraged to complete all 4 weeks of the programme. The presentation will endeavour to provide a more detailed overview of the CHOICE Programme, CHOICE delivery, and results and programme feedback.

Reference

1. Coates *et al* (2013) Evaluation of the effectiveness of a structured Diabetes Education programme (CHOICE) on Clinical Outcomes for Adolescents with Type 1 diabetes: A randomised control Trial. J Diabetes Metab, Vol 4, Iss 6.

DOI: 10.1530/endoabs.85.DPD4.2

Diabetes Main Day Sessions

Diabetes Symposium 4

DMD1.1

Abstract Unavailable

DOI: 10.1530/endoabs.85.DMD1.1

DMD1.2

Closed-loop system data review: universal approaches for treatment optimisation

Julia Ware
Wellcome Trust-Medical Research Council Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom. Department of Paediatrics, University of Cambridge, Cambridge, United Kingdom

Hybrid closed-loop systems for managing type 1 diabetes are now available and rapidly being integrated into routine clinical practice. Insulin delivery is automated in a closed-loop system via an algorithm that uses CGM data to direct insulin delivery via an insulin pump, but users need to carbohydrate count and give pre-prandial insulin to achieve optimal outcomes. Understanding the principals of closed-loop insulin delivery, and how it differs from traditional insulin pump therapy, is key to supporting and educating children and young people with type 1 diabetes using these systems. Additionally, healthcare professionals need to be able to provide specific guidance and help set realistic expectations about an increasing number of different systems available. Structured approaches to closed-loop data review are essential for post-initiation reviews and therapy optimisation. This presentation reviews basic concepts of closed-loop insulin delivery, shows universal approaches to reviewing closed-loop data, and highlights capabilities and key similarities and differences of current systems with tips for optimisation.

DOI: 10.1530/endoabs.85.DMD1.2

DMD1.3

Developing an early stage treatment for diabetic retinopathy

Tim Curtis
Queen's University of Belfast, Belfast, United Kingdom

Diabetic retinopathy is a serious complication of diabetes that can lead to vision loss and blindness. With the prevalence of diabetes rising in children, the number of young people at risk of developing diabetic retinopathy is expected to increase in the coming years. Current treatments for diabetic retinopathy only target the end-stages of the disease when significant retinal damage has already occurred. Thus, there remains an unmet medical need for new treatments, particularly those with efficacy in the early stages of the disease. Our group have recently shown that retinal accumulation of the acrolein-derived advanced lipoxidation end-product, FDP-lysine (N -(3-formyl-3,4-dehydropiperidino-lysine) plays an important role in the pathogenesis of diabetic retinopathy. We have also identified a drug called 2-HDP that is effective in scavenging acrolein and preventing retinal FDP-lysine accumulation during diabetes. In this talk, I will present our most recent data exploring the pre-clinical effects of 2-HDP on the development of experimental diabetic retinopathy. Our findings so far suggest that acrolein scavenging drugs like 2-HDP could provide an effective means to halt the development of diabetic retinopathy before it reaches its advanced, sight-threatening, stages.

DOI: 10.1530/endoabs.85.DMD1.3

Diabetes Symposium 5

DPD2.1

Abstract Unavailable

DOI: 10.1530/endoabs.85.DPD2.1

DMD2.2

Abstract Unavailable

DOI: 10.1530/endoabs.85.DMD2.2

DMD2.3

How to create and adapt exercise plans when using continuous glucose monitoring (CGM) and automated insulin delivery systems (AID) with type 1 diabetes

John Pemberton
Birmingham Childrens Hospital, Birmingham, United Kingdom

Introduction
The World Health Organisation (WHO) recommends (1) 60-minutes of moderate to vigorous physical activity per day, (2) Three vigorous sessions of aerobic activity per week, and (3) Limiting sedentary time. Despite well-evidenced benefits, population activity levels for children and young people (CYP) fall well below WHO recommendations. CYP with type 1 diabetes (T1D) added challenges, such as fear of hypoglycaemia and inadequate healthcare professional support. Technology promises to make activity and exercise more manageable, but only if health care professionals can adapt the education provided.
Aim
To explain the impact of different types of activity on glucose levels and educate on how to create and adapt activity plans for CYD with T1D using Continuous Glucose Monitoring and Automated Insulin Delivery System (AID)
Methods
Review the recent ISPAD/EASD consensus statement on exercise and CGM and the recent AID and exercise review by Zahareiva *et al*.
Results
Key messages presented (1) 10-15 minutes of moderate activity drop the glucose level by ~2.0 mmol/l (40 mg/dl). Teaching this using the mnemonic GAME in a CGM structured education program has been shown to improve time in range (TIR, 3.9-10.0 mmol/l or 70-180g/dl) (2) Educate that trend arrows to inform movement in the next 10 minutes, not 30 minutes (3) How to change carbohydrate suggestions based on trend arrows (4) How to make and adapt plans for CYP using injections and pump therapy (5) How to create plans for CYP using AID paying particular attention to (a) Less percentage bolus reductions before and after exercise (b) Setting the exercise target 90 minutes before exercise, or just before if forgotten (c) Unlikely to need an exercise target overnight (d) Drip feed smaller amounts of carbohydrate during exercise (6) There is significant inter and intra-individual variation in glucose response to the same exercise depending on insulin, nutrition and fitness conditions, and (7) Use the principle of *"the glucose never lies"*; if the glucose stays in target, it works, so don't change it.
Conclusion
Encourage as much activity as possible for CYP with T1D and make exercise management plans, explaining they will need adaptation through trial and error.

DOI: 10.1530/endoabs.85.DMD2.3

Nurses' Day for Endocrine Professionals Sessions

Endocrine Symposium 3

NEP1.1

CAH & adolescent gynaecology – an MDT perspective

Hazel Learner, Philomena Da Silva & Louise Williams
UCLH, London, United Kingdom

We work in a service at UCLH in London which cares for young people and adults with differences of sex development. Among other diagnoses CAH makes up quite a lot of our cohort of patients. Adolescents with CAH that our team see include those born with atypical genitalia who may have had, or have not had surgery in childhood on their clitoris or vagina. We also see adolescents with CAH who have issues with puberty and their periods. For adolescents with issues with their genitals (vagina/clitoris) we think about how this affects them and consider surgical options (eg. surgery to open the vagina/to reduce the side of the clitoris). We will talk about the experiences we hear from young people- those who have needed further surgery after having had early surgery, those unaware that they had genital surgery as a baby, and those who didn't have surgery in childhood. As we care for young people 12+ years, we will be discussing the experience a young person may have in coming to clinic, how we talk to young people about genitalia and how they are thinking and feeling. We know lots of young people can feel very worried or anxious about talking about their genitalia, the thought of being examined or having not very nice memories of being examined in the past. We will talk through our approach if a young person is considering genital surgery and describe our process as an MDT to allow young people to make an informed decision for what feels right for them. We will mention some of the current issues regarding early surgery not being available and the implications going forward but we will be focusing on our patient cohort.

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NEP1.2

Abstract Unavailable

DOI: 10.1530/endoabs.85.NEP1.2

NEP1.3

'Handing over the reins'- CAH and adolescence from a parent's perspective

Joanne Hall

Joanne has two adolescent daughters with salt wasting CAH. Her talk will focus on CAH during this stage of transition and aims to inform on three areas: direct insight from her daughters on key matters for adolescents living with CAH and what they need; the changes for parents; and reflections on the long-term impact on parents raising children with CAH - how can professionals help?

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Endocrine Symposium 4

NEP2.1

Immune dysregulation driving future risk of disease in children with obesity

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Obesity is linked to an increased risk of 13 different cancers in adulthood. The environment supporting this increased risk is multi-factorial but includes metabolic dysregulation, chronic inflammation and the loss of the anti-tumour activity of cells such natural killer (NK) cells. We present data which shows that this pro-cancer environment starts early in children with obesity, potentially increasing their risk of future disease. We investigated a cohort of 50 children with obesity and 50 healthy peers, and report significant metabolic dysregulation (e.g. insulin resistance), elevated inflammatory mediators (e.g. TNFa) and defective NK cell functionality (e.g. cytotoxicity). We provide evidence that altered nutrient availability in obesity underpins these alterations. Armed with this knowledge we set about investigating if GLP-1 analogue therapy could reverse the pro-cancer environment observed in obesity. We present data which shows that GLP-1 therapy significant reduces inflammation in cohorts of children with obesity (in vitro) and adults with obesity (in vivo). We show for the first time that GLP-1 analogue therapy rescues NK cell effector function in adults with obesity, independent of weight loss. We also provide evidence that GLP-1 can improve the functionality of NK cells from children with obesity in vitro. Collectively we present data which supports the presence of an obesity related pro-tumour environment in children with obesity, which we postulate may increase future risk of disease. We also show for the first time that GLP-1 therapy can attenuate this pro-tumour environment, supporting its use early in the life course of obesity.

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Oral Communications

Oral Communications 1

OC1.1

Defects in QSOX2, a novel regulator of STAT5B nuclear import and transcriptional activity, lead to severe post-natal growth restriction

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Background
Growth Hormone Insensitivity (GHI) is characterised by short stature and functional IGF-I deficiency associated with normal/elevated GH levels. Marked genetic and phenotypic heterogeneity exist, and heritable defects in GH-IGF-I axis associated pathways account for mild-moderate to severe GHI. We report non-consanguineous twin brothers who present with short stature and bi-allelic mutations in *QSOX2* encoding a nuclear membrane protein. Genome-wide association studies have identified the LHX3-QSOX2 locus as a significant height quantitative trait locus. We hypothesise QSOX2 is a novel regulator of STAT5B nuclear translocation.
Methods
Variant constructs generated by mutagenesis of an N-terminal FLAG tagged-QSOX2 cDNA were expressed in HEK293-hGHR cells. QSOX2 and STAT5B cellular localisation were assessed by immunoblotting/immunofluorescence. Nano-luciferase complementation and dual luciferase reporter assays evaluated QSOX2-STAT5B interactions and GH-induced transcriptional activity, respectively. Mitochondrial morphology and membrane potential of patient fibroblasts were examined by confocal microscopy and TMRE assays.
Results
Monozygotic twin brothers presented with severe growth restriction, immunodeficiency, relative macrocephaly, mild dysmorphism, recurrent infections, oral feeding aversion and gastroparesis. Blood profiling revealed low IgM levels and elevated basal levels of phosphorylated STAT5 compared to controls. Next generation sequencing revealed compound heterozygous variants in *QSOX2*; a novel paternally inherited single base deletion, predicted to result in a frameshift truncation and a maternally inherited missense variant, predicted deleterious in silico. We demonstrated a direct interaction between QSOX2 and STAT5B. Nano-luciferase complementation assays revealed attenuation of the interaction of both mutants with STAT5B when compared to wild type. Both mutations led to robust tyrosine phosphorylation of STAT5 following GH agonist stimulation with concomitant cytosolic accumulation and attenuation of nuclear translocation of STAT5B. This effect was phenocopied in patient-derived dermal fibroblasts and similar to the *STAT5B* p.Gln177Pro mutant which disrupts the CCD, suggesting that this domain is integral for interaction with QSOX2. Both mutants exhibited reduced STAT5B downstream transcriptional activity. A distinct mitochondrial phenotype was also observed in patient fibroblasts.
Conclusion
We describe a definitive role of QSOX2 in modulating human growth, broadening the GHI spectrum. Deficiency of QSOX2 impairs STAT5B downstream activity and mitochondrial dynamics leading to a unique syndrome of postnatal growth failure and mild immunodeficiency.

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OC1.2

A rare case of short stature with high total insulin like growth factor 1 (IGF-1) and a novel pregnancy-associated plasma protein A2 (PAPPA2) gene mutation

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Background
PAPP-A2 is a protease which helps to release IGF-1 from a ternary complex by cleaving the IGF binding proteins (IGFBP-3 and -5). Free IGF-1 subsequently binds to its receptor resulting in cell proliferation and growth. Homozygous loss-of-function *PAPPA2* mutations lead to low IGF-1 bioavailability and postnatal short stature (SS). Recombinant human IGF-1 (rhIGF-1) treatment improves height SDS in few patients. We report a patient with SS and high plasma total IGF-1 and IGFBP3 levels secondary to PAPPA2 deficiency.
Case report
A 12.3 years old girl of Jordanian origin presented to the endocrine clinic with SS and generalised delayed dental development. She was born at term with a birth weight of 2.5 Kg. There was no other past medical history of note. Her parents were non-consanguineous. Mid-parental height was 157.2 cm (9th-25th centile). 2 siblings (17 and 15 years old) were of normal stature. Her height was 134.2 cm (-2.3 SDS) with a BMI 20.1 (+0.59 SDS). There were no dysmorphic features. She was pubertal with Breast stage 3. Bone age was advanced by 1 year. Blood biochemistry showed markedly elevated serum IGF-1 level of 183.2 nmol/l (+4.9 SDS) and elevated serum IGFBP3 level of 7.1 mg/l (+1.9 SDS). CGH microarray testing was normal. Initial SS gene panel testing including *IGF1R* gene was negative. A trial of recombinant human growth hormone did not show a noticeable increment in height velocity (3 cm/year). Further testing on an extended custom short stature gene panel revealed a novel homozygous frame-shift mutation in the *PAPPA2* gene c.1223delT, p.L408Rfs*49. As she is now post-menarchal and reaching her final height, rhIGF-1 therapy is not being considered.
Conclusions
Growth failure in PAPP-A2 deficient patients is variable with height SDS ranging from – 3.8 to -0.96. Biochemically it causes a decrease in free IGF-1 but elevated total IGF-1 and IGFBP3 levels. Delayed dentition is seen as a consistent feature of this condition. PAPP-A2 deficiency should be considered and the *PAPPA2* gene should be studied in all children with SS and persistently elevated serum IGF-1 levels but with negative genetic analysis for the *IGF1R* gene.

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Oral Communications 2

OC2.1

Coeliac disease presenting with anti-OPG antibody mediated childhood osteoporosis and response to bisphosphonate therapy

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Background
Children with undiagnosed coeliac disease are at risk of low bone mineral density (BMD), but whether this translates to fracture predisposition is unclear. In adults with coeliac disease anti-osteoprotegerin (anti-OPG) antibodies have been identified. OPG inhibits RANK ligand activation of osteoclastic bone resorption, and thus anti-OPG antibodies promote bone loss. We report a case of osteoporosis with elevated anti-OPG antibodies in a child with coeliac disease.
Case
An 11-year old boy presented with a 6-month history of back pain. There was a prior history of low-trauma fractures but no family history of osteoporosis or fracture. Sclerae were white and dentinogenesis imperfecta was not present. Radiographs demonstrated extensive thoracic and lumbar vertebral compression fractures. Investigations for secondary osteoporosis revealed elevated tissue transglutaminase antibodies (anti-tTG) despite no reported symptoms of coeliac disease. Dual-energy X-ray absorptiometry (DXA) demonstrated whole body and lumbar spine BMD Z-scores of -2.0 and -4.2, respectively. Duodenal biopsy confirmed coeliac disease, and a gluten-free diet (GFD) was commenced. Bone biopsy showed a borderline mineralisation defect with mild osteopenia compatible with malabsorption. An osteogenesis imperfecta gene panel (comprising COL1A1, COL1A2, IFITM5 and those listed in the 100,000 genomes project) was normal. Anti-OPG antibodies were performed due to the reported association with coeliac disease; these were elevated at 65ng/mL (normal range <33ng/mL). Treatment with intravenous zoledronate (0.05 mg/kg every six months) was commenced. Anti-tTG normalised with gluten-free diet. Serial DXA scans have demonstrated progressive increase in BMD (BMD Z-scores at 15.6 years old: whole body 0.4, lumbar spine -0.6). There have been improvements in vertebral morphometry, no new vertebral fractures, and marked improvement in bone pain. He is approaching final adult height on the 50th-75th centile (target range 9th-91st centile). He has not sustained any further low-trauma fractures.
Conclusion
Undiagnosed coeliac disease is an uncommon cause of childhood osteoporosis, but this diagnosis should not be missed. To our knowledge, multiple vertebral fractures have not previously been reported as the presenting feature of childhood-onset coeliac disease. Confirmation of anti-OPG antibodies supports coeliac disease as the cause of osteoporosis in this patient. Bisphosphonates, in combination with GFD, were effective at improving bone outcomes.

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OC2.2

The missing segment from the age of enlightenment

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Case report

An 11-year-old boy presented with an increasingly waddling gait and backache. He had been born small for gestational age (BW 1.8kg; -4.7 SDS) and had a history of dyspraxia and autism. He reported reasonable dairy intake and had no history of previous fractures or clinical signs of osteogenesis imperfecta (OI). Spinal imaging revealed multiple vertebral fractures. Malignancy and systemic inflammatory causes were excluded. An OI gene panel revealed a single pathogenic PLOD2 variant, but as a second variant was not identified the osteoporosis could not be attributed to Bruck syndrome. Bone biopsy showed high turnover osteopenia which was not typical of Juvenile Idiopathic Osteoporosis (JIO) but could represent early-stage disease. Given his clinical picture of multiple vertebral fractures and low bone density (lumbar spine BMAD -2.0 SDS, Total body less head -2.0 SDS), he was treated as JIO. Treatment with three monthly pamidronate was commenced; in combination with physiotherapy and hydrotherapy this led to a significant clinical improvement. One year later he was changed to six monthly Zoledronic acid infusions. However, at this time he developed increasing bone and muscle pains, swollen joints and reduced mobility requiring the use of a wheelchair. This was followed by pain in the gums; osteonecrosis of the jaw (from bisphosphonates) was excluded by the specialist dental team. The bone biochemistry was normal apart from a low ALP of 100 (128-420) and coeliac screen negative. He developed a mild anaemia. Clinical photographs showed enlarged gums, a swollen knee and some bruising. Further enquiry revealed an increasingly selective diet. In combination with the bone and muscle pains, low ALP, anaemia and gum hypertrophy a diagnosis of scurvy was suspected. This was confirmed with a low Vitamin C of $<$3.0umol/l (26.1-84.6). There was a remarkable improvement within two weeks of commencing an over-the-counter preparation of Vitamin C.

Conclusions

JIO and hypovitaminosis C are two rare and unrelated conditions. JIO is a diagnosis of exclusion and managed with bisphosphonates. Nutrient deficiencies such a Vitamin C should be considered as an alternative or contributory factor if clinically indicated or if there are ongoing generalised systemic symptoms.

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Oral Communications 3

OC3.1

A rare form of ovotesticular difference of sex development (DSD) in combination with severe early-onset obesity due to MC4R mutation: clinical features and diagnostic challenges

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Background

We describe a patient with 46XX ovotesticular difference of sex development (DSD) due to 46XX/69XXY gonadal mixoploidy, also an *NR5A1* variant, who developed severe early-onset obesity and subsequently a pathogenic *MC4R* variant was identified.

Case Presentation

A term Caucasian baby weighing 3.64kg with non-consanguineous parents presented with atypical genitalia (Prader Stage 2-3) with clitoromegaly, perineal urethral opening, normal vaginal opening, bilateral inguinal herniae and masses palpable in the labio-scrotal folds. Pelvic ultrasound identified a normal uterus and indeterminate gonads in the labio-scrotal folds. Adrenal androgens were within female normal range: DHEAS 8.8umol/l (0.86-16.5) and testosterone 2.5nmol/l (1.7-5.6nmol/l). However, values in the male range were found for AMH (280.2pmol/l; 390-1300pmol/l) and inhibin (149ng/l; 128-300ng/l). Blood karyotype was 46XX and CGH array normal. DSD-panel genetic testing identified a novel heterozygous variant c.389C$>$T in *NR5A1* (nuclear receptor subfamily-5). This was not considered clinically significant as at a different location to *NR5A1* variants previously associated with 46XX and 46XY DSD and also identified in the patient's father. Female sex of rearing was agreed following multidisciplinary team (MDT) and family discussion, and inguinal herniae repair surgery was planned. At laparoscopy a bipolar right gonad was noted and biopsied; histological examination demonstrating both ovarian tissue and seminiferous tubules and karyotyping identified 46XX/69XXY mixoploidy. Further studies confirmed one X chromosome was maternally derived, the other X and Y chromosomes paternally derived. The left gonad was normal ovary, karyotype 46XX. Developmental progress was normal and general health excellent except for escalating weight gain and hyperphagia from the age of 2 years. Aged 4, weight was 115.6kg ($>$99.6thcentile), height 115.6 cm ($>$ 99.6thcentile) and BMI 25.5kg/m^2 (BMI-SDS $+$4.2). A targeted gene panel for early-onset obesity identified a pathogenic *MC4R* heterozygous variant c.105C$>$ A, p.(Tyr35*). She is receiving intensive weight management MDT input.

Discussion

46,XX/69,XXY gonadal mixoploidy is extremely rare, previous cases having male phenotype with either normal testicular development, undervilirisation or ovotesticular DSD. This in combination with a pathogenic MC4R variant causing hyperphagia and severe obesity is unique and previously unreported. This case highlights the importance of expert MDT management in complex cases and the role of dedicated gene panels.

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OC3.2

Two cases on the carney complex spectrum secondary to PRKACA/ PRKAR1A variants presenting with cushing syndrome in childhood

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Introduction

We present two cases of Carney and Carney-like Complex due to genetic aberrations with the cAMP/PKA pathway presenting with ACTH-independent Cushing Syndrome (CS) and extra-adrenal features.

Case report

Case 1 was referred aged 4 years with a 15 month history of cyclical CS (periodic weight gain, facial roundness, hirsutism). Neuroimaging did not identify a pituitary abnormality. Biochemistry confirmed ACTH-independent hypercortisolism, with a low ACTH and loss of the cortisol circadian rhythm. She was commenced on metyrapone at a dose tailored to cortisol production. Initial hypertension improved. Adrenal imaging was inconclusive. Tumour markers were negative. Genetic analysis demonstrated a heterozygous pathogenic *PRKAR1A* variant (c.491_492del) confirming a diagnosis of Carney Complex type 1. She proceeded to undergo a laparoscopic bilateral adrenalectomy, and commenced lifelong adrenal hormone replacement. Extra-adrenal manifestations of Carney Complex included cutaneous pigmentation, eye lesions and thyroid cysts. Case 2 was referred aged 3 months with unusual non-tender, non-pigmented firm lumps on his hands and feet. A month later, he developed rapid-onset hyperphagia and hypertension. Examination revealed a Cushingoid, obese (98th centile), and short ($<$0.4th centile) infant. ACTH-independent CS was confirmed biochemically. Adrenal imaging did not reveal any adrenal abnormalities. The CS was refractory to medical management and a laparoscopic bilateral adrenalectomy was performed, followed by adrenal hormone replacement. Histopathological examination of the adrenal tissue and the peripheral dermatological lesions revealed bilateral non-pigmented micronodular cortical hyperplasia and cutaneous mucinosis, respectively. CGH analysis of these affected tissues demonstrated a mosaic *PRKACA* duplication not present in the peripheral blood.

Discussion

We describe two cases of Carney and Carney-like complex secondary to genetic alterations within the cAMP/PKA pathway. Case 2 is the first time somatic, rather than germline, *PRKACA* mosaicism has been associated with micronodular hyperplasia, with cutaneous mucinosis being a novel finding. Delays in the diagnosis of paediatric CS can occur due to the rarity of the condition, its occasionally cyclical nature, and the often equivocal findings on adrenal imaging. A clinical diagnosis might only be confirmed following genetic testing. Whilst bilateral adrenalectomy treats CS, Carney and Carney-like Complex are rare multiple neoplasia syndromes, necessitating ongoing tumour surveillance.

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Oral Communications 4

OC4.1

Pseudohypoaldosteronism case series

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Pseudohypoaldosteronism is a rare salt-wasting disorder of infancy characterised by hyponatraemia, hyperkalaemia and metabolic acidosis, with increased plasma

renin activity and elevated aldosterone concentrations (1). We present three recent cases.

Case 1

An 8 day old female infant presented with poor feeding and vomiting. She was born to consanguineous parents. She was bradycardic, hypothermic and clinically shocked. Initial bloods showed hyponatraemia (sodium 116 mmol/l), hyperkalaemia (potassium >10 mmol/l) and metabolic acidosis. ECG revealed brief, unsustained runs of ventricular tachycardia. She required PICU admission. Further investigations revealed a markedly elevated aldosterone (45200 pmol/l) and renin (>34ng/ml/h), with normal cortisol and 17-OHP; suggesting a diagnosis of pseudohypoaldosteronism (PHA) - genetic testing was sent in view of consanguinity.

Case 2

An 11 week old male infant referred with faltering growth, poor feeding and frequent vomiting. Initial bloods showed significant hyponatraemia (sodium 103 mmol/l) and hyperkalaemia (potassium 6.9 mmol/l). The infant was dehydrated but normotensive and normoglycemic. Aldosterone (2891pmol/l) and renin (>500u/U/mL) were elevated with normal cortisol and 17-OHP. Urine grew Klebsiella pneumoniae and an ultrasound renal tract demonstrated right renal pelvic dilatation to 11mm.

Case 3

A 16 week old male infant also referred with faltering growth, otherwise well with no significant history. Initial sodium 124 mmol/l and potassium 6.3 mmol/l. The infant was hypotensive but glucose was normal. Again, aldosterone (>27800 pmol/L) and renin (>5000u/U/mL) were high with normal cortisol and 17-OHP. Urine grew Coliforms and an ultrasound renal tract demonstrated left renal pelvic dilatation to 10mm with dilation of the left ureter to the level of the VUJ. Given this biochemical picture important differential diagnoses include congenital adrenal hyperplasia, aldosterone synthase deficiency and adrenal hypoplasia congenita; which result in aldosterone deficiency. The genetic condition PHA-I is a heterogeneous syndrome that includes at least 2 clinically distinguishable entities with either renal or multiple target organ defects (MTOD). Case 1 is an example of MTOD PHA-I which shows autosomal recessive inheritance and is characterised by salt wastage from the salivary and sweat glands, respiratory tract and colon. Transient forms of pseudohypoaldosteronism can occur in infants with pyelonephritis and obstructive uropathy, as demonstrated by cases 2 and 3.

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OC4.2

Treatment-induced neuropathy of diabetes: a case report

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Case report

A previously well 16 year old female presented with a one day history of being unwell with agitation and confusion on the background of a three month history of polydipsia and polyuria. Initial biochemistry was in keeping with severe diabetic ketoacidosis (DKA): pH-6.75, HC03- 2.6 mmol/l, blood glucose- 21 mmol/l and ketones >4 mmol/l. Hypokalaemia of 3.3 mmol/l. She was admitted to ICU given the severity of DKA, biochemical disturbance and altered mental state. HbA1c was 157mmol/mol (16.5% DCCT) at diagnosis. Eight weeks after diagnosis, her HbA1c had improved to 62mmol/mol (7.8% DCCT). At this time she presented with acute onset burning pain in both feet, worse at night and unresponsive to simple analgesia. On discussion with the adult diabetic team a diagnosis of treatment-induced neuropathy in diabetes (TIND) was made and treatment with duloxetine and naproxen was initiated. Her symptoms resolved in three months.

Discussion

TIND is an acute, painful neuropathy that develops after rapid improvements in glycaemic control in individuals with longstanding hyperglycaemia. TIND is distinct from diabetic neuropathy due to its acute onset and often reversible nature. Neuropathic symptoms include pain, burning or allodynia. It can also be associated with autonomic dysfunction and microvascular complications. A decrease in HbA1c (glycosylated haemoglobin) of more than 2% points in 3 months, in individuals with chronic hyperglycaemia, leads to increased risk of TIND. Other risk factors include a high baseline HbA1c, female gender and weight loss. The current standard of care remains supportive.

Conclusion

TIND is an iatrogenic complication due to rapid improvements in glycaemic control in patients with diabetes. Symptoms of TIND are seen in up to 10% of adult patients with diabetic neuropathy. The prevalence of TIND in the paediatric population is unclear as literature is based solely on case reports [3]. Increased awareness and recognition of TIND in the paediatric population is required. Prospective mechanistic and therapeutic studies are needed to identify the pathophysiology and treatment of TIND.

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Oral Communications 5

OC5.1

Can lymphocyte subsets and B cell cytokines predict clinical response to Rituximab in paediatric graves' disease?

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Background

Relapse rates in young people with Graves' disease (GD) are around 75% after 2 years of antithyroid drugs (ATD). However, there is little mechanistic insight into the pathophysiology of relapse and a lack of robust predictive biomarkers. B cell subsets and related cytokines may reflect humoral immune activity, for which T cells have an important supporting role.

Aims

The purpose of this study was to evaluate T and B cell subpopulations, along with B-cell activating factor (BAFF) and soluble B-cell maturation antigen (sBCMA) concentrations as prognostic markers for predicting clinical response in young GD patients treated with ATD and the B-cell depleting agent, Rituximab (RTX).

Methods

Adjuvant RTX was administered with a 12-month course of ATD in 27 paediatric GD patients. Serum BAFF and sBCMA were investigated at baseline prior to RTX, and 12 months later. B and T lymphocyte subsets were evaluated in the 24 months following RTX. The relationship between cytokines and lymphocyte subpopulations were determined and the association with clinical outcome investigated.

Results

Disease relapse within 12 months after ATD withdrawal occurred in 14 (52%) patients. One year after RTX, BAFF and sBCMA levels had decreased from baseline ($P=0.005$, $P=0.03$, respectively), with a significant decline of BAFF observed only in relapse patients ($P=0.005$). At baseline, BAFF was negatively correlated with switched memory B cells (CD19+CD27+IgD-) (rs=-0.81, $P=2.5$ x 10-6). CD3+T cells increased following RTX ($P=0.028$). The baseline CD4/CD8 ratio was associated with relapse ($P=0.04$), which remained significant in multivariate analysis adjusted for age, gender and baseline TRAb titre (OR 2.04 95%CI 1.58-700; $P=0.04$). There was a significant increase in the CD4/CD8 ratio after ATD was stopped ($P=0.03$).

Conclusion

A greater decline in BAFF levels after RTX may indicate a poor clinical response in young people with GD. The negative association of BAFF with switched memory cells may provide mechanistic insight into GD relapse. An elevated CD4/CD8 ratio has been proposed as a marker of disease activity in paediatric GD, and in this study was found to be a prognostic biomarker, independent of TRAb titre.

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OC5.2

Central Delayed Puberty in Adolescence: Differentiating the phenotypes of Congenital Hypogonadotropic Hypogonadism and Self-Limited Delayed Puberty

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Congenital hypogonadotropic hypogonadism (CHH) is a pathological condition characterised by lack of pubertal onset and must be differentiated from self-limited delayed puberty (SLDP). There is a significant overlap between these two conditions both in clinical and biochemical features, with current diagnostic

approaches lacking sensitivity. Thus, paediatric endocrine clinicians are faced with difficulty in ascertaining the correct diagnosis in adolescence. The presence of certain red flags - cryptorchidism and micropenis in males, anosmia or midline defects may indicate gonadotrophin deficiency, but these signs are frequently absent, particularly in patients with partial CHH phenotypes. Published data from our group demonstrated the utility of whole exome sequencing in differentiating CHH from SLDP in our UK cohort. In this project, we analysed the phenotypic and genomic data of patients presenting in adolescence with central delayed puberty who had reached 18 years, with a final diagnosis of CHH or SLDP. We aimed to define a pragmatic scoring system based on clinical, biochemical and genotypic data to enable accurate diagnosis between these two conditions. Eighty patients with pubertal delay, from two separate datasets, were included in this study. A scoring system was developed from 46 patients (13 CHH, 33 SLDP) in Dataset 1 (2015-2020). Five key clinical parameters (testicular volume $<$3mls, cleft lip or palate, anosmia, micropenis or cryptorchidism, family history of SLDP or CHH), alongside biochemical markers (Inhibin-B and AMH) together with genotypic score (1-5 based on variants of interest in known SLDP or CHH genes) were included in a predictive score (maximum points 13 in males, 11 in females) to estimate the likelihood of CHH. This scoring system was fine-tuned and validated in a second group of 34 patients (19 CHH, 15 SLDP) (Dataset 2, 2020-22). Final diagnosis of CHH or SLDP correlated with score in 88% (30/34) of patients in Dataset 2. By utilising a diagnostic score, we were able to accurately differentiate patients with CHH from SLDP at presentation in the large majority of this study. A combined clinical, biochemical and genetic scoring system may thus provide a useful approach to improve diagnostic accuracy and management for patients with central pubertal delay.

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OC5.3

UK protocol for induction of puberty with gonadotropins in males with hypogonadotropic hypogonadism

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Hypogonadotropic hypogonadism (HH) is a rare reproductive disorder that results in a lack of normal pubertal development and reduced potential for fertility in adult life. The condition is characterised by low circulating sex steroid concentrations resulting from a deficiency of pituitary gonadotropin production. HH may be congenital or acquired, most commonly due to tumour or treatment for malignant disease. When associated with anosmia it is termed Kallmann syndrome. HH is also seen as part of a syndrome or alongside other pituitary hormone defects. Induction of puberty in male adolescent patients with HH has traditionally been with low and increasing doses of testosterone from the age of 12 years. However, whilst this management can induce virilization, it will not promote testis growth nor the potential for spermatogenesis. Recent robust evidence has demonstrated the efficacy and tolerance of the use of subcutaneous human chorionic gonadotropin (hCG) together with recombinant follicle-stimulating hormone (rFSH) to induce male puberty. Particularly for those with cryptorchidism and pre-pubertal testicular volumes, pre-treatment with rFSH is important to promote expansion of the Sertoli cell population to optimise capacity for sperm production. At present there is no national or international guideline for pubertal induction with gonadotropins in males with HH. A recent BSPED survey ($n=18$, from 13 centres) showed interest in a suitable guideline in 100% of responders and that the current barrier to gonadotropin use for this indication is lack of expertise or protocol in 88%. Through a multicentre approach, we have developed a practical protocol for paediatric endocrinologists for induction of puberty in male patients with this condition. The protocol includes two separate arms for patients with testes volumes of $<$ or $\geq$ 6mls, with pre-treatment with rFSH in the former group and initial monotherapy with hCG in the latter group (with addition of rFSH as required). Parameters for monitoring, dose adjustments and management of side-effects are addressed. In summary, we present an evidence-based multicentre developed guideline for the induction of puberty with gonadotropins in males with HH, which can be used in tertiary endocrine settings across the UK to improve fertility outcomes in this patient group.

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OC5.4

Greater postnatal adiposity gain following inadequate fetal growth in the manchester babyGRO study

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Background
Previous studies use small for gestational age (SGA) as a surrogate marker for fetal growth restriction (FGR). SGA individuals, particularly those who show catch-up growth have greater cardiometabolic (CM) risk than those born appropriate for gestational age. However, not all FGR fetuses are born SGA. Therefore, we studied neonates born following pregnancies at increased risk of FGR, irrespective of birthweight.
Aim
To define associations between fetal weight trajectory and postnatal weight and adiposity trajectories from birth to six months.
Methods
Participants were recruited from a specialist clinic of women considered at increased risk of FGR, based on maternal antenatal serology (pregnancy associated plasma protein-A $<$0.415 multiples of the median (MoM), alpha fetoprotein $>$2.2 MoM or inhibin A $>$2 MoM). Births $<$34 weeks' gestation were excluded. Measurements were taken for weight, length, mid-upper arm circumference (MUAC), abdominal circumference (AC), thigh circumference (TC), and biceps, triceps and subscapular skinfold thicknesses. Body mass index (BMI, weight(kg)/(height(m))^2) and the sum of skinfolds (sum SF, mm) were calculated. ΔfetalC ([birthweight centile minus 23 week estimated fetal weight centile]/days) and postnatally, ΔweightC ([six-month weight centile minus birthweight centile]/days), as well as ΔBMI, sum SF, MUAC, AC and TC were calculated. Pearson's product moment correlation coefficient (parametric) and Kendall's tau (non-parametric) were used to determine correlations between ΔfetalC and ΔweightC, BMI, sum SF, MUAC, AC and TC.
Results
Of 42 participants with ΔBMI data available, 36 (81%) had a negative ΔfetalC, but only 3 (7%) were born SGA. ΔfetalC correlated negatively with ΔBMI ($r=$ -0.38, $P=0.012$), sum SF ($r=$-0.36, $P=0.016$, $n=43$), MUAC ($r=$-0.32, $P=0.034$, $n=44$) and AC ($r=$-0.30, $P=0.045$, $n=44$), but not with ΔweightC or TC.
Conclusions
ΔfetalC was negatively linked with postnatal markers of adiposity in early life, highlighting inadequate fetal weight gain as an indicator of accelerated postnatal adiposity. Only a small proportion were SGA, suggesting that FGR should be considered an independent risk factor for CM risk. The absence of an association between ΔfetalC and ΔweightC demonstrates the value in monitoring adiposity changes in the first six months. Therefore, routine postnatal length measurements to calculate BMI are necessary.

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OC5.5

The lack of genotype: phenotype correlations in rare causes of primary adrenal insufficiency highlights the need for genetic testing

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Background
Primary adrenal insufficiency (PAI) can be associated with significant morbidity in children of all ages, the most common cause being Congenital Adrenal Hyperplasia (CAH). Several other rare inherited causes of PAI have been identified over the years which lack diagnostic phenotypic or biochemical signs, leaving genetic testing as the only approach to make a definitive diagnosis. Our cohort involves $>$440 patients who presented with features of PAI – hypoglycaemia, hyperpigmentation and hypocortisolaemia without diagnostic characteristics of CAH. Targeted and whole exome sequencing has been conducted in 377 patients to date.
Aim
Genotype:phenotype characterisation for our cohort's five most common genes causing PAI.

Results
We identified the genetic cause in 322/377 patients, the most common being mutations in MC2R ($n=68/322$), MRAP ($n=53/322$), NNT ($n=44/322$), STAR ($n=28/322$) and CYP11A1 ($n=23/322$). The relative risk of early age of onset of symptoms with an MRAP mutation as compared to other gene mutations causing PAI within our cohort was 1.5158 (95%CI: 0.9988-2.3003, $P<0.05$). Comparing the cortisol levels, individuals with MRAP mutations have the lowest (difference = 303.54 nmol/l; 95%CI: 225.15-381.93, $P<0.0001$) while those with CYP11A1 variants have the highest levels (difference = 223.44 nmol/l; 95%CI: 122.70 – 324.18, $P<0.0001$) amongst our cohort. For CYP11A1 2/4 (50%) adrenals were described as small whereas for all others only 11/102 (11%) were abnormal. No other significant association with height or levels of other steroids were found between the genotypic and phenotypic characteristics of PAI.
Discussion
A limitation of this study was the small sample size for each gene defect owing to the rarity of the disease. Our results suggest MRAP mutations present the earliest with lowest cortisol, while CYP11A1 have higher cortisol and smaller adrenal size however, with overlapping ranges this cannot be used for diagnosis. For CYP11A1 the higher cortisol levels may be due to over-representation of partial loss-of-function rs6161 variant in our population. These findings also highlight the importance of genetic testing since few clear genotype:phenotype correlations are obvious at diagnosis. Gaining a genetic diagnosis allows for the monitoring of patients for the pathological sequelae which can develop with different forms of PAI.

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OC5.6

Prevalence of overweight and obesity in children with bone fragility and its correlation with disease severity and fracture rate

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Aims
To examine, in children with Osteogenesis Imperfecta (OI): the prevalence of overweight and obesity, longitudinal trends in body mass index (BMI) z-scores and total body fat percentage (TBF) assessed on dual-energy X-ray absorptiometry (DXA) scans, correlation between BMI and TBF and fractures and BMI z-score.
Methods
Retrospective cross-sectional and longitudinal analysis of children with OI, with minimum 5 years data on DXA scans, at a single nationally commissioned OI service. Data was gathered on severity of OI, number of fractures (long bone and vertebral) during study period, BMI, BMI z-scores and TBF. Obesity and overweight were defined in accordance with the UK-WHO growth standard criteria. The cohort was categorised into pre-pubertal (6-8 years), pubertal (9-14 years) and post-pubertal (15-18 years). A t-test and Kruskall-Wallis test was used to compare groups and categories respectively. Pearson's test was used to assess correlations.
Results
A total of 54 patients (55.6%, $n=30$ males) were included. The majority ($n=44$, 81.5%) had mild OI (G1) and rest moderate/severe (G2) ($n=10$,18.5%). 25.9% ($n=14$) were obese and 33.3% ($n=18$) overweight. In G1 and G2 the prevalence of obesity was 27.3% and 20% respectively and of overweight was 27.3% and 60% respectively. The mean BMI z-score at baseline (mean age 8.4 years) in G1 and G2 was (+0.49 and +1.02 respectively; $P>0.05$) similar. At the most recent visit (mean age 14.2 years) the mean BMI z-score was higher in G2 compared to G1 (+1.92 vs +1.06 respectively; $P=0.04$). The pre-pubertal, pubertal, and post-pubertal mean BMI z-scores were +0.33, +1.03 and +1.5 respectively ($p<0.001$) and mean TBF were 30.9%, 36.0% and 38% respectively ($p<0.001$). There was a significant correlation between BMI and TBF ($r=0.813$, $P=<0.001$). The BMI z-score was significantly correlated to the number of long bone fractures ($r=0.28$, $p<0.001$) but not vertebral fractures ($P=0.6$).
Conclusion
Children with moderate/sever OI had a higher BMI in the post-pubertal years and this tendency was correlated to long bone fracture rate. Awareness of risk factors provides the opportunity to intervene early. Monitoring TBF on DXA scans is useful when clinical assessment of BMI is challenging.

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OC5.7

Salivary cortisol and cortisone in healthy children and young people

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Background
Cortisol is inactivated to cortisone in the salivary gland by 11β-HSD type 2. Concentrations of cortisone and cortisone in saliva correlate strongly with serum cortisol concentrations (1). Only free, biologically active hormone is measured in saliva, testing is non-invasive and can be performed at home/school, reducing cost and inconvenience to families and NHS resources. We previously reported pilot data from healthy children and young people (CYP) (1). Here we describe salivary cortisol (SC), and cortisone (SCn) concentrations, and SCn:SC ratios in a larger cohort.
Methods
Healthy CYP children aged 5-18 years old participated. Exclusion criteria: Medical conditions and medications that may affect cortisol concentrations, family history of inherited adrenal disorders and oral lesions. Samples were collected 30 mins after waking and at 2-hour intervals thereafter, until sleep. Patients did not clean their teeth or eat one hour before sampling. Samples were analysed by LC-MS/MS.
Results
86 (49M) participants, median age for males was 10.8years (IQR = 5.6), median female age was 11.0 years (IQR = 4.7). 7 samples at 7 time-points collected. 8hours after waking, SC was undetectable in 3 samples (3.5%), after 10 hours in 11 samples (12.9%) and in 24(28.3%) samples after 12hours. SCn was always detectable. SCn:SC was 4.2 (1.60) on the waking sample and increased throughout the day to peak 10 hours after waking, 9.8 (3.62). Mean area under the curve (AUC) for SC was 28.7nnmol/l (95%CI 13.0-44.3) for females and 27.0nmol/l (95%CI 12.6-41.5) for males, $P=0.0136$. AUC for SCn in females was 170.9nmol/l (95%CI 120.5-221.3) and 154.8nmol/l (95%CI 106.3 - 203.2) in males $P=<0.0001$. When correlated with age using Pearson r, SC was 0.08 ($P=0.48$) and SCn was 0.07 ($P=0.5$).
Conclusion
Data from this larger cohort confirm our previous findings. SC is often undetectable and SCn may be a more reliable measure. SC and SCn are related to sex but not age. The ratio of SCn:SC increases through the day, suggesting that the circadian cortisol profile is regulated partly by changes in the relative activity of 11β-HSD type 1 and 2.
Reference
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OC5.8

SGPL1 deficiency impairs Leydig cell steroidogenesis and should be considered in 46XY individuals with DSD and adrenal insufficiency

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Sphingosine-1-phosphate lyase 1 insufficiency syndrome (SPLIS) is a multi-systemic syndrome in which primary adrenal insufficiency (PAI) and steroid resistant nephrotic syndrome predominate, secondary to loss-of-function mutations in SGPL1 (sphingosine-1-phosphate lyase). SGPL1 carries out the irreversible breakdown of sphingosine-1-phosphate, a bioactive sphingolipid intermediate, with implicated roles in various cellular processes. Wider endocrinopathy including gonadal insufficiency and hypothyroidism are described. We aimed to conduct a retrospective analysis to determine the extent of gonadal insufficiency in our SPLIS patient cohort and the wider literature and develop an in vitro model to study the potential impact of SGPL1 on gonadal steroidogenesis. A third of male patients presented with primary gonadal insufficiency (all with concomitant adrenal disease), with microphallus and bilateral cryptorchidism, suggestive of reduced androgen exposure in utero. Where tested, individuals showed an exaggerated response during LHRH stimulation and poor androgen response to HCG stimulation. All, excepting 1 individual, died in early infancy with multi-systemic disease. Mortality in the condition is high (approximately 50% in childhood) and in those surviving male patients pubertal delay has yet to be reported. No impact on gonadal function has been reported in girls with the condition. Accordingly, we generated CRISPR-

engineered knock-out (KO) of Sgpl1 in the MA10 immortalised Leydig cell line. Sanger sequencing confirmed a single base 'A' insertion in Exon 7, predicting a frameshift mutation and premature stop codon in the KO clone. This was further validated by western blotting demonstrating loss of SGPL1 expression in the KO as compared to wild type (WT). WT and KO cell lines were stimulated with forskolin for 6 hours, with significantly reduced progesterone production seen in the KO. This was associated with decreased steroidogenic enzyme STAR and CYP11A1 expression by western blotting, both in unstimulated and forskolin stimulated conditions in the KO Leydig cells. MTT assays also demonstrated decreased cell proliferation in the KO cell line.
Conclusion
SGPL1 deficiency should be considered in the differential diagnosis of 46XY infants with differences in sex development (DSD) and PAI. SGPL1 deficiency impairs steroidogenesis in Leydig cells and clinicians need to be mindful of evolving gonadal disease in patients with SPLIS.

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OC5.9

Evaluation of a low postnatal hypoglycaemia threshold

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Background and objective
Neonatal hypoglycemia is common and frequently self-resolving, although rare due to congenital hyperinsulinism are associated with high risk of brain injury. The time period for neonatal hypoglycemia has been described in several studies. It is unknown if low hypoglycemia thresholds (<2.0 mmol/l) lead to missed cases of persistent hypoglycaemia. We aimed to ascertain if lower hypoglycemia threshold risked missing persistent forms of hypoglycemia in a large cohort.
Design and setting
We evaluated glycaemic outcomes of all neonates (17594 glucose measurements) in the postnatal wards of a large maternity center over one year.
Results
A total of 17594 blood glucose levels (48 measurements per day) were undertaken in the postnatal wards from 2749 neonates. For all values, the mean (95% CI) glucose was 5.99 (5.95-6.03) mmol/l with 5th centile and 95th centile values at 2.37 and 11.00 mmol/l respectively. Frequencies for various hypoglycaemia cut-off levels (mmol/l) were: <3.0 (10.1%); <2.6 (5.8%); <2.2 (2.9%); and <2.0 (2.2%). Blood glucose <2.0 mmol/l occurred in 239 neonates. In all neonates, glucose levels improved on retesting [1.50 (1.45-1.55) to 3.16 (3.05-3.26), $p<0.001$]. In 239 neonates with hypoglycaemia (glucose <2.0 mmol/l), higher mean (95%CI) glucose levels [1.61 (1.57-1.65) vs 1.05 (0.93-1.17)] were associated with lower risk of re- admission [$p<0.001$]. Follow-up assessments were available for 39 neonates and none were readmitted with hypoglycemia later.
Conclusion
Hypoglycaemia is frequent in neonates with point of care testing detecting blood glucose less than 2.0 mmol/l in just over 2%. A low hypoglycaemia threshold of 2.0 mmol/l in the early period, was not associated with later life persistent hypoglycaemia. The low postnatal hypoglycaemic threshold in current practice can be continued, although careful monitoring is required due to the risk of escalation to persistent hypoglyaemia due to disorders such as Congenital hyperinsulinism. Our findings demonstrate the relative utility of carefully monitored low postnatal hypoglycemia threshold.

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Oral Communications 6

OC6.1

Pubertal staging examinations: a national survey of current practice in consent and chaperone use

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Background
General Medical Council (GMC) guidance describes an intimate examination as one that may be embarrassing for the patient, for example, breast or genitalia examination. Documentation of consent and use of a trained impartial observer (chaperone) is recommended for intimate examinations. Pubertal staging is often necessitated for assessment of growth and puberty. We assessed current practice in pubertal staging by paediatricians and paediatric endocrinology nurse specialists (PENS) in the United Kingdom.
Methods
An electronic survey was distributed to paediatricians (consultants and trainees) and PENS across the UK during May and June 2022. The survey enquired about training received, confidence in and typical practice for pubertal staging examinations.
Results
235 responses were received (117 consultants, 95 trainees and 23 PENS; 74.9% female). Low confidence in pubertal staging was commonly reported by trainees and consultants without an endocrinology interest. Most respondents consider pubertal staging to be an intimate examination for males (94.9%) and females (93.1%). 77.9% were aware of the GMC guidance on intimate examinations, but only 33.6% had read this. 186 respondents perform pubertal staging. Consent to examination is always documented by 38.2% of respondents, usually/occasionally documented by 37.1% and never by 24.7%. More respondents who had read the GMC guidance always documented consent (54.5% vs 29.2%, $p<0.001$). 62.0% and 54.8% report always using a chaperone for male and female pubertal staging, respectively. Male respondents are more likely than females to always use a chaperone for female pubertal staging (85.4% vs 43.4%, $p<0.001$), whereas similar proportions of male (58.3%) and female (62.7%) respondents use a chaperone for male pubertal staging. 63.4% and 65.4% would use a parent as chaperone for male and female examinations, respectively. Few document the name of the chaperone used. Ease of finding and availability of chaperones were the most commonly reported barriers to use.
Conclusions
Most clinicians consider pubertal staging an intimate examination, but documentation of consent and use of formal chaperones is not standard practice. The use of a parent as a chaperone was common but is not recommended by the GMC. Local chaperone policies should address these issues to protect patients and clinicians.

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OC6.2

The Arginine-nitric-oxide pathway links suboptimal fetal growth to higher childhood systolic blood pressure in the manchester babyGRO study

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Background
Cardiometabolic (CM) risk is linked to being small for gestational age (SGA, birthweight $<$-2SDS). Suboptimal fetal growth alone may be linked with greater CM risk without resulting in SGA. Therefore, we focused on CM risk in children born following pregnancies at higher risk for growth restriction, irrespective of birthweight.
Aims
1. To identify associations between fetal and childhood weight trajectories and CM risk markers. 2. To define molecular pathways associated with CM risk.
Methods
We recruited 81 children aged 3-6 years, following term pregnancies at increased risk of growth restriction based on maternal antenatal serology (pregnancy associated plasma protein-A <0.415 multiples of the median (MoM), alpha fetoprotein >2.2 MoM or inhibin A >2 MoM). Body mass index (BMI) SDS, abdominal circumference (AC), mid-upper arm circumference (MUAC), %fat, systolic blood pressure (SBP) and brachial augmentation index (AI) were recorded. With consent, fasting blood samples were collected for CM markers and 'omics analyses ($n=31$). Δfetal ([birthweight centile minus 23-week estimated fetal weight centile]/days) and Δchild ([weight centile minus birthweight centile] /years) were divided into quartiles and differences in CM markers compared between Q1 and Q4. Differentially expressed genes (DEGs) and metabolites (DEMs) were established using EdgeR and MetaboAnalyst. Gene set enrichment analysis (GSEA), a method used to identify over-represented genes within a set, enabled identification of pathways.
Results
69% (56/81) had Δfetal <0, but only 12% (10/81) were born SGA. SBP was higher and HDL lower in Δfetal Q1 (lowest intrauterine weight gain) vs Q4 (highest intrauterine weight gain). SBP, BMI SDS, AC, MUAC, AI and %fat were higher in Δchild Q4 (highest childhood weight gain) vs Q1 (lowest childhood weight gain) (all $p<0.05$). GSEA based on DEGs between Δchild quartiles

highlighted a pathway including *ARG1*. Ornithine was a DEM between Δfetal quartiles and also Δchild quartiles.
Conclusions
Low Δfetal and high Δchild were associated with CM risk, with a less favourable CM profile after pregnancies with suboptimal fetal growth. 'Omics analyses uncovered the arginine-nitric-oxide pathway, which has previously been associated with hypertension. Ornithine and *ARG1* could represent early-life indicators for hypertension in later-life.

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OC6.3

Use of 24 weekly decapeptyl SR in central precocious puberty is well-tolerated and efficacious – a two centre study

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Central precocious puberty (CPP) is a common and well-recognised condition characterised by premature activation of the hypothalamic-pituitary-gonadal axis, with consequent potential adverse health and psychosocial outcomes. Standard management of CPP is with periodic injections of gonadotropin-releasing hormone analogue therapy. Decapeptyl SR (Triptorelin pamoate) has for several years been available as a long-acting (12-weekly, 11.25 mg) preparation, but more recently is available as a 24-weekly (22.5 mg) preparation. We aimed to examine the efficacy and tolerance of this 24-weekly Decapeptyl preparation in our clinical CPP cohorts at the Royal London Children's Hospital (RLH) and Royal Victoria Infirmary Newcastle (RVI). We completed a cross-sectional cohort study and patient questionnaire in each centre. The current patient cohort at the RLH consists of 56 patients treated with 12-weekly Decapeptyl, 12 (11 female, 1 male) of whom have converted to 24-weekly Decapeptyl. The RVI cohort consists of 66 patients (59 female, 7 male) that have been treated solely with 24-weekly Decapeptyl, and 18 (15 female, 3 male) who were treated with 12-weekly first and then converted to 24-weekly Decapeptyl. Analysis of the cohort data suggested that the 12-weekly and 24-weekly Triptorelin preparations have a similar efficacy, with biochemical evidence of luteinising hormone (LH) suppression in 82% of patients on the 12-weekly preparation and 99% of those on the 24-weekly regime ($P = 0.25$, 95% CI -1.325 to 0.3748). The median change in Tanner breast stage post treatment was +0.4 in the 12-weekly group and -0.22 in the 24-weekly group ($P = 0.1495$, 95% CI -0.2485 to 1.493). There was also no significant difference in post-treatment height, height velocity or BMI between the two groups. Overall, the results demonstrated no significant difference in efficacy between the 12-weekly and 24-weekly preparations. 100% of patients that completed the questionnaire indicated that the less frequent injection schedule was preferable, suggesting that adopting the 24-weekly treatment into clinical practice would be well received. In addition, in view of the equivalent dose cost of the 24-weekly preparation, there is an estimated cost saving due to the reduced clinic time required to administer this preparation.

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OC6.4

A Collaborative community based approach in providing support for children and young people with severe obesity

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Background
The highest rates of childhood obesity are among children from lower socioeconomic groups. Tier 3 weight management services for children currently rely on an MDT approach that is focused on the management of complications associated with excessive weight, but the resources are generally limited. Evidence suggests that the input in the community is key to empower children, young people, and their families to make healthy lifestyle changes, although the availability of these programmes are patchy and variable across the country. We present the experience from a successful partnership with an external charitable organisation in providing community support for weight management for a group of children and adolescents with severe obesity.
Methods
A collaborative partnership (MOVE plus project) was established between the Tier 3 weight management service, the Hospital, and the external partner (Liverpool Football Club Foundation) following a successful (Premier League) funding application. The governance structure incorporating data sharing regulations and a referral pathway was established following which children and young people managed as part of Tier 3 MDT weight management service were recruited into the project. The suitability of patients was assessed during MDT evaluation. The health coaches in the project delivered a combination of 12 virtual and in-person (based at the community hubs) physical activity sessions. Patients were offered 12 low-moderate intensity exercise sessions alongside dietary advice covering topics such as portion sizes, food labelling and energy balance. Participants completed Food frequency questionnaire (FFQ) and Commitment to Physical Activity and Children's Attitude toward Physical Activity (CAPTA) pre and post programme. Patients and their families reported positive behavioural changes post intervention and stated they felt more empowered to engage with the Tier 3 MDT weight management advice.
Conclusion
Collaborative weight management interventions show promise for effectiveness and acceptability by patients, families, and care providers. More research needs to be carried out to review the long-term effectiveness of these services. External partnerships that could provide local support especially in socioeconomically deprived communities would be of great value to families and help achieve strategies to promote healthier choices, thereby bridging the gap between the health care and community sectors.

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OC6.5

Bone mineralisation as assessed by bone health index in children with congenital adrenal hyperplasia

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Background
21-hydroxylase deficiency congenital adrenal hyperplasia (CAH) is characterised by cortisol deficiency, androgen excess, varying degrees of virilisation and salt-wasting. CAH management involves replacement therapy with hydrocortisone, and, often, fludrocortisone. High levels of androgens cause the advancement of bone age (BA) with the potential to increase bone mineralisation. Hydrocortisone therapy on the contrary can contribute to reducing bone mineralisation. Patients with CAH have an increased prevalence of fractures which may be related to bone mineralisation.
Objectives
To assess whether bone mineralisation in paediatric CAH patients is significantly different to the general population and to determine factors contributing to bone mineralisation.
Methods
Bone health index (BHI) measured using BoneXpert provides observer-independent information on cortical thickness and mineralisation based on hand X-ray and correlates with bone mineralisation measured by Dual-energy-X-ray-absorptiometry. 141 (74 female, 67 male, 0.32 – 17.55 years) records of CAH patients at Royal Manchester Children's Hospital were accessed and data collected for z-scores of bone age (BA), bone health index (BHI), height, weight, body mass index (BMI), adrenal androgens and renin; hydrocortisone (HC, mg/m2/day) and fludrocortisone (FC, mg/m2/day) doses were also collected. One sample t-tests were undertaken for variance in growth parameters, BA and BHI standard deviation scores (SDS) compared to the normal population; correlation was assessed between BA SDS, BHI SDS, and adrenal androgens, renin, HC, and FC doses.
Results
BHI is significantly reduced (mean -0.5, $p < 0.001$) while BA is significantly advanced (mean 2.6, $p < 0.001$). No correlation was found between BHI and HC dose, FC dose, adrenal androgens (except for negative correlation between BHI and DHEAS) (Table).

Conclusion
Bone mineralisation as assessed by BHI, in our cohort, is reduced and this may contribute to increased prevalence of fractures in CAH. This deficit appears to be independent of adrenal androgen levels and HC dosing.

Parameter against BHI	N	Correlation Coefficient	Significance
HC	50	r(48) = -0.05	0.723
FC	46	r(44) = -0.10	0.516
17OHP	46	ρ(44) = 0.193	0.200
Androstenedione	42	ρ(40) = -0.03	0.841
DHEA-S	34	ρ(32) = -0.51	0.002
Testosterone	48	ρ(46) = 0.09	0.542
BA	45	r(43) = 0.31	0.036

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Oral Communications 7

OC7.1

Comparison of outcomes of the hybrid closed loop therapy with the conventional insulin pump in the first year after pump initiation

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Introduction
Hybrid closed loop (HCL) therapy has been shown to improve the glycaemic control in children and adolescents with Type 1 Diabetes. There is however limited data comparing the HCL therapy with conventional insulin pump therapy. We aimed to retrospectively compare the outcomes of hybrid closed loop (Tandem T slim) and conventional insulin pumps.
Methodology
Electronic patient records for all the patients using insulin pump therapy at Sheffield Children's Hospital were reviewed (98 patients). Data for 62 patients (between November 2016 to November 2021) were analysed. 8 patients on HCL who had previously been on a conventional pump were excluded. Mean or median HBA1c prior to starting the pump were compared with values at six weeks, six months and Twelve months between the groups using paired-T test. We also compared TIR, Hypoglycaemia, variability over the duration of one year.
Results
Results from 22 patients with HCL (mean age-9.25years, mean duration of diabetes -23 months) and 34 patients with conventional pump (mean age-7.5years, duration of diabetes -12 months) were compared. Median HBA1C in the HCL group decreased from 54.5 ± 8.4 mmol/mol at baseline to 49.4 ± 7.5 mmol/mol at 6 months ($P = 0.242$) and 51.0 ± 6.3 at one year (P-0.1723) after pump initiation. HBA1C in the conventional pump therapy improved from 53.7 ± 7.39 to 52.9 ± 8.8 at 6 months with no change at 12 months. The Average TIR (3.9-10 mmol/l) measured by Dexcom CGM in the first year was 49% with HCL compared to 44.9% with the conventional pump. No DKA was recorded in these groups. The variability did not change between the groups over one year (37% and 37.5%). HCL group had lesser hypoglycaemia (3.1%) compared to 4.1% in conventional group.
Conclusion
Patients with Hybrid closed loop had a better Time in range and lesser incidence of hypoglycaemia. There was an improvement of HBA1C with the Hybrid closed loop noted at 6 months and one year. HCL appears to have a better performance with only a modest improvement in HBA1C, likely due to the smaller sample size and/or good diabetes control prior to pump initiation.

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OC7.2

Self-collection of capillary blood samples at home for HbA1c measurements during the COVID-19 pandemic in children with diabetes mellitus

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Background
Rapid implementation of tele-clinics was necessary during the COVID-19 pandemic. Patients missed routine point-of-care HbA1c testing, vital for evaluating long-term glycemic control. We evaluated the feasibility of remote HbA1c monitoring via self-collection of capillary blood samples at home, and examined clinical characteristics associated with patient engagement.
Methods
Bio-Rad Haemoglobin Capillary Collection System (HCCS) was used, with kit performance tested at the Chemical-Pathology Laboratory at Royal London Hospital. 100 participants were recruited from paediatric diabetes clinics at 2 East London sites (4-19y, Pre-Covid HbA1c:29-120mmol/mol). Home kits for capillary sample self-collection were mailed out with step-by-step instructions and video demonstration links, with a prepaid envelope for sample return. Feasibility was assessed by the rate of sample return and time taken for sample arrival at the laboratory. A usability survey addressing the home collection process and user-experience was emailed to all families, consisting of 7 questions on a 5-point Likert scale to assess ease of use and preferences around HbA1c monitoring.
Results
Completion rate was 58%. Mean duration from kit being mailed out to sample analysis was 15.6 ± 9.8 days (median:13.5). Pre-covid HbA1c was higher in the group that failed to return a sample, as compared to the group that did (65.3 ± 20.1 vs 56.8 ± 14.7 mmol/mol, $p < 0.05$). Overall, HbA1c remained relatively stable over the pandemic in the completion group (T1DM: 60.1 ± 8.8 to 57.1 ± 8.8, $P > 0.05$, T2DM: 56.4 ± 28.8 to 52.4 ± 17.3, $P > 0.05$). A higher proportion of non-T1DM patients had an increase in HbA1c over the pandemic (T1DM ($n = 41$) : 49%, T2DM ($n = 8$): 63%, Other ($n = 5$): 80%). Usability scores were high: 96% found it easy to learn capillary blood sample collection, and 89% found this system very convenient.
Conclusion
Self-collection of capillary blood samples at home is a feasible option to remotely monitor HbA1c in patients with stable glycemic control and good prior engagement with their care. Routine telemedicine appointments could be suitable and convenient for these patients, utilising data from their continuous monitoring devices. Future work would improve processes such that HbA1c level is regularly available prior to the telemedicine appointment, and to assess and remove hurdles for engagement to increase completion.

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OC7.3

Hypogonadism and pubertal disorders in wolfram syndrome

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Background
Wolfram Syndrome (WS) is a rare autosomal recessive disorder characterised by early-onset diabetes and optic atrophy as well as a variable spectrum of other endocrine and neurological conditions. It is caused by mutations in the WFS1 gene. Previous reports have documented a variable prevalence of hypogonadism (6.3% of the international EURO-WABB registry, 34% of a German cohort); however the only UK cohort reported was of 10 males, 7 of whom had primary gonadal atrophy (Barrett *et al* 1996)
Aims
To review the prevalence of hypogonadism and pubertal disorders in a national cohort of children and young people (CYPD) attending the NHSE highly specialised multidisciplinary (MDT) service for paediatric WS.
Methods
Retrospective case review of all CYPD with WS seen in a single paediatric centre with documented WFS1 mutations since 2012. Electronic records were assessed for documented testicular volumes, age of menarche and menstrual irregularities as well as gonadotrophin, testosterone and oestrodiol levels
Results
38 patients aged between 10-22 years (19M: 19F) were assessed. In males, of those who had completed puberty ($n = 15$), 2 (13.3%) complained of erectile dysfunction, 3 (20%) had testicular volumes < 4mls aged 14 years and 3 (20%) required testosterone replacement therapy, 6 (40%) showed evidence of hypogonadism. In females, of those who had achieved menarche ($n = 18$), 5 (27%) had evidence of irregular periods and 2 (11%) had menorrhagia requiring treatment. 1 (6%) had evidence of delayed puberty.
Discussion
In this contemporary UK cohort, the range of pubertal abnormalities in both males and females is significant with a high proportion of females reporting menstrual

problems even with a normal puberty. This may cause particular issues in young women with multiple sensory deficits. The proportion of young male patients with hypogonadism and/or erectile dysfunction is also high and points to a wider phenotypic spectrum of gonadal abnormalities than previously suspected. Young people with Wolfram syndrome should have a full pubertal assessment and that of gonadal function as a baseline, with hormone replacement and psychosexual counselling as necessary.

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OC7.4

Type A insulin resistance syndrome presenting with PCOS features and an unusual pattern of diabetes in a 10-year-old female

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Background
Type A insulin resistance syndrome (TAIRS) is rare (prevalence 1/100 000) and is caused by pathological mutations in the insulin receptor (INSR) gene. The clinical features tend to affect females more severely. Patients can present with severe hyperinsulinemia, hyperandrogenism and acanthosis nigricans. We report a case of a girl with symptoms initially suggestive of polycystic ovarian syndrome (PCOS) but also with asymptomatic diabetes mellitus.
Case
A 10-year-old female presented with severe hirsutism, acanthosis nigricans and glycosuria though asymptomatic for diabetes. At presentation the patient's height was 149.2 cm (95th centile), weight 45.5 kg (91st centile) and body mass index (BMI) of 20 kg/m2. The HbA1c was elevated at 56 mmol/l but fasting glucose levels were in normal range (4.4 mmol/l). A serum insulin (2530pmol/L) and C-peptide levels (2806pmol/L) were markedly increased. Continuous glucose monitoring showed a profile of post-prandial hyperglycaemic but paradoxical hypoglycaemic episodes in the early mornings. Testosterone (9.8 mmol/l) and androstenedione (25.1 mmol/l) were extremely elevated. Pelvic ultrasound showed grossly enlarged ovaries with an appearance consistent with PCOS (right ovary: 51x21x27 mm, vol 15 ml; left ovary: 59x23x25 mm, vol 18ml). Genomic analysis revealed a heterozygous missense mutation in the INSR gene on chromosome 19 (Pro1205Leu), diagnostic of TAIRS. The patient was managed with Metformin 500 mg in the morning to which she was very sensitive and after 6 weeks of treatment had also halved her testosterone levels (4.7 mmol/l). However as this was still very high for a girl of her age, she was then also commenced on cyproterone acetate (50μg) daily.
Conclusions
An unusual but characteristic glycaemic pattern of both post-prandial hyperglycaemia and early morning hypoglycaemia (unlike type 1 and 2 diabetes), in combination with symptoms of severe hyperandrogenism is suggestive of TAIRS and would indicate the need for genetic testing. Currently there is no specific management to target the underlying genetic mutation and therefore management is symptomatic control. Pharmacological therapy for insulin resistance using Metformin may be very beneficial.

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OC7.5

Monogenic obesity is probably not so rare - experience from a large tier 3 paediatric weight management service

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Background
Monogenic obesity is generally considered to only be responsible for a small proportion of genetic obesity with the vast majority attributable to polygenic obesity. Previous studies estimate that monogenic obesity accounts for less than 5% of obesity in Caucasian populations.
Aims and method
To identify prevalence and clinical characteristics of monogenic obesity, we reviewed clinical notes of 219 patients currently, or recently (within 24 months), under the care of a tier 3 childhood obesity service. In those with positive genetic results, testing was mostly performed using targeted obesity gene panels or by CGH array in a minority of patients for another clinical reason. Genetic testing for monogenic causes was particularly considered in patients with early-onset obesity before 5 years of age or defining clinical features. Prader-Willi and Beckwith-Wiedemann syndrome were excluded from the analysis.
Results
In a cohort of 219 patients, we identified 26 with mutations in single genes and 2 with specific chromosomal deletions implicated in early onset obesity. Overall, the prevalence of monogenic obesity in our cohort was 12.7%. *MC4R* mutations were the most frequent monogenic cause. Of these 28 patients, mean parentally-reported age of onset of obesity was 19.3 months (range 6-48 months) and mean age of referral to our service was 7.1 years (range 1-15 years). Mean BMI-SDS in these patients was +3.45 (range 1.90-5.45). 19/28 (67.8%) patients had hyperphagia, 14/28 (52%) behavioural difficulties and 3/28 (11%) a diagnosis of autism. 17/28 (60.7%) patients had a family history of obesity.
Discussion
Diagnosis of genetic obesity is important as some forms have personalised treatment (e.g. Setmelanotide for LEPR, PCSK1, POMC) and may help reduce stigma. Monogenic obesity is probably not as rare as previously described, increasingly being detected by targeted gene panels. Onset under two years of age, hyperphagia, behavioural problems and family history of obesity should raise suspicion of monogenic obesity.

	Gene involved	Number of Patients
Mutations	MC4R	11
	PCSK1	3
	GNAS1	2
	NTRK2	2
	POMC	1
	ALMS1 (Alstrom syndrome)	1
	BBS1 (Bardet-Biedl sundrome)	1
	INSR	1
	KSR2	1
	LDLR	1
	MAGEL2	1
	SIM1	1
Chromosomal deletions	16p11.2 deletion	1
	22q11.21 deletion	1
	Total	**28**

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OC8.1

Do we need earlier thyroid surveillance amongst PTEN patients in the UK?

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Background
Germline mutations in the Phosphatase and Tensin Homolog Hamartoma tumour (PTEN) gene are associated with a number of conditions, collectively known as PTEN hamartoma tumour syndromes (PHTS). Individuals with PHTS are at increased risk of a number of cancers primarily in adulthood including differentiated thyroid carcinoma (DTC) with an estimated lifetime risk of DTC of up to 38%. International guidance recommends screening commencing from 17 years while the 2017-UK national guidelines recommend from 16 years. At our centre, we perform annual thyroid ultrasound scan surveillance from 10 years within a dedicated endocrine tumour clinic.
Aim
To assess the value of the thyroid surveillance screening in the < 18-year paediatric population with PTEN.
Methods
A single centre retrospective study at Birmingham Women's and Children's Hospital. All children with germline mutations in the PTEN gene ($n=30$) were identified over last fifteen years. Children under 10 years at the time of study were excluded ($n=10$) from analysis. Assessment was through electronic health records for genetic diagnosis, comorbidities and results of their thyroid imaging
Results
16/20 (80%) had at least one thyroid ultrasound. 8/16 (50%) had significant findings on scan that needed further investigation (additional scan, FNAC or biopsy). Thyroidectomy was recommended in 3/8 (38%). Two children (2/16,

12%) had benign histopathology. One (1/16; 6%) child had DTC (papillary). His first thyroid ultrasound scan was at fourteen years of age confirming right sided growth. He initially underwent right thyroidectomy followed by total thyroidectomy after confirmation of malignancy on histopathology.

Discussion

In our single centre study, 1 child (6%) had a diagnosis of DTC under the age of 18 years which was successfully treated with surgery. This could have been missed if surveillance had commenced at 16 years. Surveillance findings on scan which are benign can cause parental and child anxiety. However, it is important to recognise that earlier thyroid surveillance may be important. More research needs to be done to improve our understanding of the risks and benefits of earlier screening.

Additional Features	
Macrocephaly	15/20 (75%)
Developmental delay	13/20 (65%)
Autistic Spectrum	12/20 (60%)
GI problems	4/20 (20%)
Penile freckling	2/20 (10%)

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OC8.2

Endocrine effects of MEK and BRAF inhibitor therapy in paediatric patients: a tertiary centre experience

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Introduction

In children, BRAF (e.g. dabrafenib) and MEK (e.g. trametinib) inhibitors are used to treat a range of tumours including low-grade gliomas, Langerhans cell histiocytosis (LCH), and plexiform neurofibromas. However, the ubiquitous nature of the BRAF/MAPK/MEK pathway in various physiological processes means that these treatments are not without their own side effects such as renal tubulopathies (causing hyponatraemia) and hyperglycaemia.

Aim

To describe the endocrine dysfunction observed in a cohort of children treated with BRAF and MEK inhibitors at Great Ormond Street Hospital, the largest paediatric centre in the UK utilising these treatments.

Methods

Electronic data for patients treated with dabrafenib and trametinib from January 2019 to May 2022 were collected. Outcomes included patient weight, BMI, BMI SDS, blood glucose, insulin and HbA1c concentrations and the presence of hyponatraemia (< 135 mmol/l).

Results

A total of 55 patients (28 males, 27 females) on dabrafenib ($n=25$) and trametinib ($n=42$) were included for analysis. The median age was 9.64 years old. The most common indications for treatment was low-grade glioma ($n=35$). Growth hormone deficiency was the most noted co-morbidity ($n=10$), followed by precocious puberty ($n=9$). Nine patients had at least one hyponatraemic episode during treatment of whom three had coexisting central diabetes insipidus. The mean minimum sodium for all patients during treatment was 136.3 mmol/l. A total of 6 patients were diagnosed with a form of glucose dysregulation (e.g. insulin resistance, type 2 diabetes), of whom four were diagnosed during treatment, all with hypothalamo-pituitary lesions.

Discussion and Conclusion

Whilst the use of BRAF and MEK inhibitors herald a new era in targeted molecular treatment for various tumours, it is also important to recognise and monitor for unique endocrine side effects in patients on these treatments.

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OC8.3

Characterisation of the first heterozygous missense HMGA2 variant helps delineate the crucial functional roles of a novel growth gene

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Background

Silver Russell syndrome (SRS) is genetically heterogenous and around 30% of patients with clinical SRS have no genetic diagnosis. Point mutations in *HMGA2* have been reported in 4 patients worldwide causing growth failure and an SRS-like phenotype. Despite strong evidence of the crucial role of *HMGA2* in growth across species, the mechanism of action of *HMGA2* in human linear growth is unclear.

Objective

Identify and functionally characterise *HMGA2* mutations in a patients with growth failure and SRS features.

Methods

We used custom bioinformatic pipelines to filter genetic data generated from our novel targeted genome short stature gene panel. Our Dutch collaborators identified further novel *HMGA2* variants of interest. Our novel missense *HMGA2* variant was functionally assessed using Electrophoretic Mobility Shift Assays (EMSAs). Our Canadian collaborators generated novel $Hmga2^{K56E}$ transgenic mice using CRISPR/Cas technology.

Results

We identified 6 novel heterozygous *HMGA2* variants in patients with growth failure and SRS features. This includes the first heterozygous missense mutation c.166A>G, p.(Lys56Glu) in a patient with pre- and post-natal growth failure, low BMI, triangular face and high arched palate; 3/6 NH-CSS. The variant was predicted pathogenic (CADD score 27.2; Mutation taster: disease causing) and was inherited from her mother who had short stature and similar facial features. This novel variant resides in a critically important region of *HMGA2*, adjacent to the second AT hook/DNA binding region. This missense variant substitutes lysine, a positively charged amino acid crucial for DNA binding at target sites, for glutamic acid, a negatively charged amino acid. EMSAs confirmed reduced binding of the mutant c.166A>G HMGA2 protein to target DNA sequences. Transgenic mice harbouring homozygous c.166A>G p.(Lys56Glu) mutations ($Hmga2^{K56E}$) displayed dysmorphic facial features similar to the phenotypes observed in SRS children. $Hmga2^{K56E}$ transgenic mice were fertile but small for gestational age and showed SRS-like dwarfism.

Conclusions

We report the largest *HMGA2* case series to date including the first heterozygous missense mutation. Binding to DNA target sites was impaired in the mutant c.166A>G HMGA2 protein. A novel transgenic $Hmga2^{K56E}$ mouse model recapitulated the SRS phenotype seen in our patient, confirming the critical functional importance of this amino acid residue.

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OC8.4

A national survey of bone-endocrine monitoring in duchenne muscular dystrophy and the patients experience

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Objectives

DMD Care UK (www.dmdcareuk.org) is a national project initiated and funded by Duchenne UK in collaboration with Newcastle University and the UK North Star clinical network. The main aim is to facilitate implementation of care standards across the UK national health system. In 2021, DMD Care UK conducted a comprehensive online family survey of all aspects of care of boys with DMD with the aim of capturing the patients experience. Here, we present results relating to bone-endocrine care.

Methods

An online survey was circulated in May 2021.

Results

164 parents/carers responded to the survey. Median age of the young person with DMD was 11 years (Range 2,46). 32/164(20%) were 18 years and older. 78/164(48%) have been seen by an endocrinologist or recently referred. Vitamin D levels were not checked regularly in 27/164(16%). 61/164(37%) have not ever had lateral spine imaging to screen for VF. 48/164(29%) undergo spine imaging every 12 months,14/164(9%) every 2 years, 34/164(21%) every 3 years or longer. 30/164(18%) have never had a DXA for assessment of bone density. Only 6/62(10%) of adolescents

aged 13-18 years had received testosterone therapy. 13/124(11%) on steroids were not aware or unsure of emergency steroid sick day dosing plans. 66/164(40%) were very satisfied or satisfied with endocrine/bone care, with 18/164(11%) who were dissatisfied or very dissatisfied. Feedback on areas that are important to the patients and influences satisfaction include a regular bone healthmonitoring programme, timely assessment of puberty, open discussions of hormone treatment for puberty/-growth and clear instructions on steroid sick day dosing plans.ConclusionThis first national survey of bone-endocrie management in DMD demonstrates variability despite the 2018 international guidance. A consistent bone health monitoring programme, timely assessment of puberty, open discussions of hormone treatment (testosterone and growth hormone) and clear instructions on management of steroid during illness are of great importance to patients in this bone-endocrine care. These are priorities to be addressed by DMD Care UK, and important points to be considered in service development.

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OC8.5

Contrast media-induced hypothyroidism

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A preterm baby was born at 23 weeks + 2 days gestation. She was managed on our tertiary care neonatal unit and remained ventilated for most of her stay. During her admission, she had recurrent episodes of clinically suspected NEC which were medically managed. Her feeds were discontinued on numerous occasions due to bilious aspirates, vomiting and abdominal distention. Given the patient's clinical condition, a barium meal was done using an enteral iodinated contrast agent to exclude a stricture. She also developed ascites and needed 4 radiologically-inserted drains. No underlying cause was found for her ascites, which spontaneously resolved over a period of 2 weeks. Her thyroid function had been normal; however, further testing 5 days following the barium meal revealed a markedly elevated TSH (>500 mU/L) with free T4 <5.2 pmol/l. Due to intestinal failure, treatment with IV levothyroxine was required. This was gradually reduced and then stopped as the patient's TFTs normalised. This case demonstrates the harmful effect of iodine-containing, radiologic contrast media on thyroid function, and the potential risks of using these contrast media in neonates with suspected intestinal failure. Intestinal failure in this case prolonged the time of exposure to the oral contrast agent. It reinforces the recent FDA-approved warning to the prescribing information for the entire class of iodinated contrast media injections and monitoring recommendations for children 3 years or younger. This FDA warning was posted in March 2022 and is available https://www.fda.gov/safety/medical-product-safety-information/iodine-containing-contrast-media-drug-safety-communication-fda-recommends-thyroid-monitoring-babies In addition, this case also demonstrates the rare need for treatment with IV levothyroxine, as the patient was not absorbing any enteral medications or feeds, secondary to intestinal failure.

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Oral Communications 9

OC9.1

Access and use of new technologies in diabetes care in patients that need an interpreter compared to those that do not

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Young people with Type 1 Diabetes Mellitus (T1DM) can achieve improved glycaemic control by using technology. T1DM technology is steadily improving however access to it remains variable across the UK. Those from ethnic minorities and deprived areas are less likely to access technology and more susceptible to developing complications of diabetes. Understanding the reasons for health inequalities is essential to facilitate use of available technology.

Aim

Review the use of available technology across our diverse population of young people with T1DM.

Method

We prospectively invited families over 3 months to participate in a voluntary questionnaire reviewing the use of technology.

Analysis

Ninety Eight families responded and 88 questionnaires were included in the analysis. Of these 35% (31/88) used an Insulin Pump and 60% (53/88) CGM. Those using pumps and CGM achieved the best HbA1c (<8%) with 70.9% (22/31) and 76% (40/53) respectively. Data was divided into two groups; those who spoke English as a first language ((EFL) $n=65$) and English as a second language ((ESL) $n=23$). Findings are summarised in Table 1. The difference between access to mobile phones was statistically significant ($p<0.005$) with 82% (18/23) in ESL compared with 97% (63/65) in EFL. Access to a home computer was similar (ESL- 78% and EFL- 88%) however a difference exists in downloading with ESL achieving 26% (6/23) whilst EFL achieved 40% (26/65). CGM was accessed in only 48% (11/23) in ESL compared with 65% (42/65) in EFL. Time in Range (TIR) was reduced and statistically significant ($p<0.05$) with TIR< 50% in 58% (11/19) in ESL compared with 32% (18/57) in EFL.

Conclusion

Technology in T1DM significantly improves HbA1c in young people however families require support and training to achieve this. Our study indicates that inequalities maybe remedied by facilitating access to phones to enable management of T1DM.

Table 1

	EFL ($n=65$)	ESL ($n=23$)	P value
Computer	57 (88%)	18 (78%)	0.273
Phone	**63 (97%)**	**18 (82%)**	**<0.005**
Insulin Pump	21 (32%)	9 (39%)	0.553
CGM/Flash	42 (65%)	11 (48%)	0.157
Downloads	26 (40%)	6 (26%)	0.233
TIR < 50%	**18 (32%)**	**11 (58%)**	**<0.05**
HbA1c<8	44 (68%)	16 (69%)	0.868

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OC9.2

Audit of management of diabetic ketoacidosis in children at the noah's ark children's hospital for wales

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Introduction

Diabetic Ketoacidosis (DKA) is a potentially 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 based on the current British Society for Paediatric Endocrinology and Diabetes (BSPED) guidelines. The BSPED guideline moved away from cautious fluid replacement toward a liberal approach for resuscitation and maintenance fluids based on current evidence. The ICP has been established in Wales with the 6th edition published in March 2022 following the NICE guideline update.

Objectives

To audit the management of DKA at the Children's Hospital following the introduction of the interim BSPED guidelines on which the 5th edition of ICP was based.

Methods

Retrospective case note review of all CYP admitted in DKA over 24 months between 01/04/2020 and 31/03/2022.

Results

A total of 20 episodes of DKA were recorded in 19 patients (14 of them were male). The median age was 13 years (range 1 to 16 years). 17 of the episodes were in newly diagnosed CYP. In all cases, the diagnosis of DKA was made appropriately per the current guidance. 11 CYP presented in mild DKA, 4 in moderate DKA and 5 in severe DKA, all of whom received appropriate fluid boluses and the fluids as recommended. Hypoglycaemia was reported in 4 of the 20 episodes whilst on the pathway, and hypokalaemia was reported in 11 of 20 episodes despite having recommended potassium in the fluids. There were no episodes of cerebral oedema.

Conclusions

The ICP was used in all cases and in general followed well. The increased incidence of hypokalemia despite following the pathway needs further evaluation and comparison with other centres using the ICP and BSPED guidance. However, no adverse outcomes were identified. We need to audit the most recent update of the ICP to recommend further changes.

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OC9.3

Diabetes and obesity in down syndrome across the lifespan: a retrospective cohort study using UK electronic health records

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Background
Down Syndrome (DS) is the commonest form of chromosomal trisomy. Genetic factors in DS may increase the risk for diabetes. Obesity and type 2 diabetes mellitus (T2DM) rates have increased in the general populationbut it is not known whether this similarly affected people with DS.
Objective
To determine whether DS is associated with increased incidence of diabetes and the relationship with obesity across the lifespan compared to controls.
Methods
Matched population-based cohort study (UK Clinical Practice Research Datalink, 1990-2020). DS patients were identified using diagnostic codes for DS or Trisomy 21; up to 4 matched controls for each DS case was selected.
Results
9,917 DS and 38,266 control patients were analysed. Diabetes rates were higher in DS individuals (incidence rate ratio 3.68; 95% CI 2.43 – 5.57; $p<0.0001$) and peaked at a younger age with over four times higher incidence per 1,000 patient years in children with DS aged 5-14 years old (1.55; 95% CI 0.95 - 2.39) compared to controls (0.38; 95% CI 0.25 – 0.57). There was over six times increased incidence of T1DM in patients with DS aged 15-24 years (1.13; 95% CI 0.62 - 1.90) compared to controls (0.18; 95% CI 0.09 - 0.33). T2DM rates were higher in DS compared to controls at age groups 5 years up to 34 years with over 10 times increased incidence in children aged 5-14 years with DS (0.62; 95% CI 0.27 - 1.22) compared to controls (0.06; 95% CI 0.02 - 0.16). In DS, peak mean BMI (kg/m2) was higher and at younger age (male = 31.2 at 31 years; female = 32.1 at 43 years) compared to controls (males = 29.5 at 54 years; females 29.2 at 51 years); obesity was associated with an increased incidence of T2DM.
Conclusions
At younger ages, the incidence of diabetes in DS patients is up to four times that of controls. Peak mean BMI is higher and established earlier in DS, contributing to T2DM risk. Further investigation into the relationship between obesity and diabetes in DS is required to inform treatment and prevention measures.

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OC9.4

Do the UK's commercially available real-time continuous glucose monitoring devices have robust accuracy data for paediatrics?

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Introduction
NICE Guidance 18 updated in March 2022 will make real-time continuous glucose monitoring (rtCGM) the standard of care and recommends the cheapest rtCGM that meets an individual's needs. Eight rt-CGM devices have Conformité Européene (CE) mark for paediatrics with type 1 diabetes. There are no published performance standards for CE mark; however, the Food & Drug Administration (FDA) published their interoperable CGM (iCGM) criterion. For iCGM approval for adults, robust standards include the 15/15 accuracy requirement for time below range (TBR, <3.9 mmol/l), time in range (TIR, 3.9-10.0 mmol/l), and time above range (>10.0 mmol/l), and the 20/20 accuracy requirement for the glucose range 2.2-22.2 mmol/l. Paediatric iCGM approval requires comparable data. However, if a CGM device has CE mark, there are no further UK accuracy safeguards.
Design and Methods
Step 1) Obtain paediatric peer-reviewed accuracy studies for the eight rt-CGMs available in the UK. Step 2) Compare each rtCGM device accuracy data against the adult 15/15 iCGM requirement; 85% of paired Yellow Spring Instrument (YSI) readings within 0.8 mmol/l (15 mg/dl) for TBR, 70% of paired YSI readings within 15% for TIR, and 80% of paired YSI readings within 15% for TAR. Compare each rtCGM device accuracy data against the 20/20 iCGM requirement; 87% of YSI readings within 1.1 mmol/l (20 mg/dl) for TBR and within 20% when 3.9-22.2 mmol/l.
Results
Glucomen Day® & Medtrum TouchCare® Nano had no peer-reviewed studies prior to CE Mark. The Medtrum TouchCare® A6 and GlucoRx AidexTM studies were excluded as all participants were adults with >80% having type 2 diabetes. The MiniMed Guardian™ Connect (7-17yrs) study data did not allow assessment against 15/15 criteria. The Dexcom G6™ (6-17yrs) only failed the 85% accuracy within 0.8 mmol/l for TBR. The Dexcom G7TM (6-17yrs) and Freestyle Libre® 3 (6-17yrs) met the selected iCGM criteria.
Conclusion
Only the Dexcom G7™ and Freestyle Libre 3™ performance meet the15/15 and 20/20 adult iCGM accuracy criteria. The Dexcom G6TM failed one measure but has been iCGM approved by the FDA as comparable. Of concern, the Glucomen Day® & Medtrum TouchCare® Nano are available without published data and the Medtrum TouchCare® A6 and GlucoRx Aidex™ without any peer-reviewed paediatric-specific data.

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OC9.5

Raising awareness of the importance of preconception counselling in young people with diabetes

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Introduction
Pregnancy under the age of 19 is considered high-risk[1]; and a pregnancy with diabetes at this age further increases that risk[2,3]. With the correct advice and counselling, these risks can be greatly reduced. Here we describe a strategy to raise awareness by addressing this as part of regular clinic visits.
Method
Prior knowledge of potential complications of pregnancy was assessed as part of a clinical consultation. Evidence-based resources in the form of articles[4,5,6] were then provided and the learning was reassessed and incorporated into the next consultation with MDT input in a caring and supportive manner. For efficiency and ease of data processing, this was facilitated through use of a multi-choice questionnaire linked via a QR code. Knowledge before and knowledge after teaching was then compared. https://docs.google.com/forms/d/e/1FAIpQLSe-dyyoWkxRaCiq3BNd4pPlfCrc4aa0pJx8ce4wwnYT6iYV4Yw/viewform
Preliminary results
The study included 5 young people with diabetes ($n=5$) and was extended to 10 young people without diabetes, so knowledge could be compared between cohorts (total $n=15$). All reported they would like to know more about diabetes and pregnancy, and only one said they were able to discuss anything about the topic. The preferred style of delivery was either articles or outside speakers for the group with diabetes, and videos for those without. Most felt any form of contraception was acceptable and underestimated the incidence of unplanned pregnancy. Only one person correctly guessed the extent of complications, while the majority underestimated the impacts. From a list of 10 possible complications, only 3 were correctly identified. Additional supplementation was inferred by less than half and only one person knew the correct daily dose. Pregnancy targets for HbA1c and time in range were little understood and nobody knew the target at which a pregnancy is ill-advised.
Conclusion
There is a clear need for education on this topic in populations with and without diabetes. A preconception counselling teaching pack incorporating feedback on preferred learning styles has now been assembled for use during clinic and the project will be extended across our wider Trust which includes over 100 adolescents; the impact of which will be reported at conference.
References
On request

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OC9.6

A review of patient outcomes and responses to weight management strategies used by complications from excess weight service, a new paediatric, hospital-based weight management service

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In June 2021, NHS England commissioned 15 Complications from Excess Weight (CEW) services to pilot Tier 3 paediatric weight management services in England. This study aimed to assess initial patient experiences / responses to weight management strategies delivered in a single CEW service between January-June 2022.

Methodology

We conducted an online survey to assess patient experiences, motivators and barriers to healthy lifestyle change in 45 patients seen. 38 patients / carers were successfully contacted by phone (maximum 2 contacts) and provided with the online survey-link and a pseudo-anonymised patient identifier. A survey response rate of 66% was received. Additionally, 12 patients who had been seen face-to-face at a 3-month review had auxology from hospital records calculated for mean change in BMI-SDS from first appointment to follow-up.

Results

The survey found 44% ($n=18$) and 34.8% ($n=23$) reporting cost as a barrier to eating healthily and engaging in physical activity respectively. Over a quarter (28%, $n=18$) had autistic spectrum disorder / learning difficulties which contributed to dietary and exercise limitation. Over a third (44%, $n=23$) reported mobility as a barrier to physical activity. Approximately two thirds (64%, $n=25$) reported weight-related bullying, nearly half (48%, $n=25$) felt uncomfortable talking about their weight and 44% ($n=25$) said their weight had negatively impacted their mental health. 60% identified improvement to mental health as a motivator ($n=25$) to making lifestyle change. In 12 patients (mean BMI SDS 3.84) seen at 3 month follow up, a mean change in BMI-SDS – 0.12 was achieved (males -0.40SDS, females -0.15SDS, primary school age -0.35SDS, secondary school age +0.10SDS). Although gender and school age differences were noted, these were not statistically significant.

Conclusions

Cost is seen as a significant barrier to healthy lifestyle change and weight management services need to look at cost effective ways of motivating patients to eat healthily and exercise effectively. Autism / learning difficulties and mobility issues also feature as significant barriers to standard management, requiring specific and tailored interventions to achieve successful lifestyle change. Finally, poor mental health is a common finding in this cohort that requires intervention to achieve better holistic outcomes for patients.

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OC9.7

Liraglutide for the treatment of severe obesity in children: early experiences from a tier 3 paediatric weight management service

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Background

Liraglutide is a glucagon-like peptide analogue recently approved for use in children and young people for treating obesity. It is recommended for use within multidisciplinary weight management services, alongside dietetic and lifestyle interventions, in children over 12 years with severe obesity.

Aim

To describe our experiences of using liraglutide in a tier 3 paediatric obesity service in a patient cohort who had previously failed to successfully lose weight despite multidisciplinary team (MDT) input.

Methods

Liraglutide was started at 0.6 mg and increased weekly as tolerated up to a maximum dose of 3.0 mg. BMI was recorded 3- and 6-months after commencing liraglutide.

Results

37 patients commenced liraglutide. Patients with treatment duration over 3 months were included in outcome analysis (23 patients; 12 female; age range 10.4-17.9 years). BMI-SDS before treatment ranged from +2.58 to +4.71 (mean +3.69). 7/23 patients had complications of obesity: hypertension (2), non-alcoholic fatty liver disease (3) and obstructive sleep apnoea (2). 7/23 patients had neurodevelopmental problems: autism (2), attention-deficit hyperactivity disorder (3) and learning difficulties (2). 22/23 (96%) patients had continued liraglutide at their 3-month review; one stopped due to pre-existing mental health problems. Gastro-intestinal side effects were frequent but mostly felt to be tolerable. 22/23 patients escalated to 3.0 mg daily but 1 remained on 1.8 mg due to significant nausea. 20/23 (87%) patients had lost weight at 3-month review (mean BMI reduction 4%; BMI-SDS change -0.13). Five patients (5/23) who had received 6 months treatment demonstrated further sustained BMI decrease (mean BMI reduction 6%; BMI-SDS change -0.24).

Discussion

These data represent encouraging results for the effectiveness and tolerability of liraglutide in adolescent patients who have not previously lost weight despite MDT input. This is promising as liraglutide is likely to become more widely used with the expansion of paediatric obesity services through the NHS-England funded complications of excess weight (CEW) clinics. Further follow-up is needed into longer-term outcomes in these patients.

Duration of treatment (months)	BMI % change (mean, range)	BMI-SDS change (mean, range)
3 ($n=23$)	-4.1 (-12.4 to +4.9)	-0.13 (-0.38 to +0.07)
6 ($n=5$)	-6.3 (-17.8 to +4.3)	-0.24 (-0.629 to +0.5)

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OC9.8

Cyclic improvement of a structured education programme teaching dynamic glucose management strategies in children and young people with type 1 diabetes using continuous glucose monitoring

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Background

In 2019, funding for continuous glucose monitoring (CGM) commenced for children and young people with diabetes (CYPD) in our region. However, there was no local established CGM structured education programme. We developed 'the CGM Academy' with continuous improvement using the Plan-Do-Study-Act (PDSA) cycle.

Objectives

To review the PDSA cycle of improvements to deliver structured education using CGM.

Methods

A CGM curriculum, using evidence-based structured education guidelines, was developed (January-February 2019). Dynamic glucose management (DynamicGM) using glucose values and trend arrows to maximise time in range (TIR, 3.9-10.0 mmol/l) was taught through 6 face-to-face (F2F) sessions. The COVID-19 pandemic necessitated virtual (V) adaptation and adoption of a "Flipped Learning" approach, truncated into three sessions, an interactive workbook with short videos, and personalised hypoglycaemia and exercise algorithms. The first 50 CYPD educated through F2F (April 2019-February 2020) and V (April 2020-February 2021) programmes were assessed for change at six months from baseline in time below range (TBR, <3.9 mmol/l), HbA1c, and TIR. Qualitative user feedback was gathered. Cost-analysis compared the F2F and V programmes. Combined data from the total cohort was analysed to identify the strongest predictors of TIR to teach the most effective strategies.

Results

The F2F cohort reduced TBR by 8.3% ($p<.001$) and HbA1c by 3.8mmol/mol ($p<.001$) and improved TIR by 9.6% ($p<.001$). User feedback indicated that the six-session programme was lengthy. The V cohort reduced TBR by 9.2% ($p<.001$) and HbA1c by 4.9mmol/mol ($p<.001$) and improved TIR by 8.9% ($p<.001$). Qualitative feedback suggested information overload from teaching too many DynamicGM strategies. There was an 18% cost-saving for every 50 CYPD educated by the V (£4,601) vs. the F2F (£5616) programme. In the combined cohort ($n=100$), the strongest predictors of TIR were: Short-bursts of exercise to stop highs, bolus timing to stay in target and a weight-based hypoglycaemia algorithm to prevent lows.

Conclusion

PDSA cycles ensured regular innovation of the CGM Academy resulting in a clinically effective cost-saving programme.

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Oral Communications 10

OC10.1

Hormone replacement therapy in paediatric turner syndrome – evaluation of current practice in a dedicated paediatric turner clinic and subsequent development of patient resources

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The British Society for Paediatric Endocrine and Diabetes (BSPED) published guidance in 2016 on optimal Hormonal Replacement Therapy (HRT) for pubertal induction in Turner Syndrome (TS). Transdermal preparations of oestrogen are the most appropriate method of oestrogen delivery in TS, as it avoids first pass metabolism of the liver, and thereby does not exert a meaningful effect on blood pressure.

Objective

To assess change in prescribing practice in accordance with BSPED guidance.

Methods

Electronic records and case note review of all girls attending a dedicated paediatric TS clinic, Royal Hospital for Children Glasgow. Data collected included date of commencing hormone replacement therapy (HRT) and oestrogen preparation used (oral ethinyloestradiol, oral 17b-oestradiol or transdermal oestrogen). Girls were consulted to determine what influenced their choice of oestrogen preparation and gauge their understanding of the aims of hormone replacement.

Results

29 girls were included who had commenced oestrogen therapy of which 24 were pre-guidance and 5 were post-guidance. 24 (100%) girls were commenced on ethinyloestradiol pre-guidance and 1 (20%) girl post-guidance (with 2 commenced on 17b-oestradiol and 2 girls commenced on transdermal oestrogen). The most common reasons offered for reticence to a transdermal preparation was fear that the patch would be visible, and doubts around how to accurately cut the patch to ensure adequate dosing.

Discussion

In response we liaised with Turner Syndrome Support Society (TSSS) to develop a video on how to prepare and apply transdermal oestrogen. This resource is available online, free of charge, for patients and their families. We have also produced a visual aid for use in demonstration/discussion with girls and their families on the available preparations of oestrogen and progesterone used in pubertal induction. The video was launched at two patient engagement zoom events hosted by TSSS to discuss the process of pubertal induction and the relative merits of the various oestrogen preparations.

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OC10.2

Patient and parent experiences with oral hydrocortisone formulations for adrenal insufficiency

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Background

The choice of hydrocortisone (HC) formulation for children with adrenal insufficiency necessitates considerations for dose accuracy, palatability, and practicality in everyday life to optimise medicine adherence and health outcomes. Recently, several diverse new formulations have become available in the UK, but no information is available on real-life patient preferences for the different formulations.

Objectives

Explore patient and parent experiences using HC, including assessment of palatability, child independence with using their medicine, barriers to adherence, and additional support required by parents.

Methods

A national web-based survey was offered to children and adolescents (0-18 years) with adrenal insufficiency or their parents, and circulated via patient support groups and locally at our centre. Taste was scored on a 7-point numerical or validated TASTY scale.

Results

There were 111 responses (77 parents; 34 children independently or together with parent). 14% ($n=15$) of parents prepared doses by dispersing HC 10 mg tablets in water rather than using smaller strength preparations. Palatability: HC tablets were rated lower than Alkindi® and liquid suspension (mean score 3.2 vs 4.1 and 4.9, respectively). For the 6-13 years age group, more responders (parents and children) using Alkindi® 'strongly agree' or 'agree' that that the doses were easy for the child to prepare independently compared to those using tablets (67% vs 27%), but there was no difference for older children. 20% ($n=22$) of responders reported missing doses due to the formulation prescribed or obtaining it via their GP or pharmacy in time. 55% ($n=61$) of responders stated they would find it 'extremely useful' to attend a steroid training clinic for a discussion of choice of HC formulations.

Conclusion

Our survey highlights the variability in national practice with use of HC formulations not matched to patient/parent needs. The real-life data show benefits of using Alkindi® for younger children to encourage independence with taking their medicine, while both Alkindi® and liquid suspension may improve adherence owing to better taste. A pharmacist-led clinic may be helpful to identify suitability of HC preparations for families to facilitate individualised choice of formulations and liaison with primary care for continuity of support across care settings.

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OC10.3

Development and testing of a novel 'Growth monitor' Smartphone App for growth monitoring and the detection of growth disorders

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Background

Growth monitoring identifies treatable conditions in apparently healthy children and prevents inappropriate referrals. Systematic growth monitoring is not currently a UK priority and growth disorders are frequently diagnosed late.

Objectives

Develop and test the accuracy of a smartphone app which enables families to measure a child's height at home as a cost-effective alternative to primary care growth monitoring.

Methods

'GrowthMonitor' app (GMA) utilises augmented reality to measure height and algorithms to determine height standard deviation score (HSDS) relative to UK population-based height references. Eligible participants were able to stand unaided, provide informed consent and had access to an iPhone compatible with the GMA (iPhone 6S-13; iOS 13.5 or later). GMA measurements were taken in parallel to stadiometer (gold standard) height measurements as part of routine clinic visits. A subset of parents used the GMA to measure their child's height at home. The target was to achieve 95% of GMA measurements within ± 0.5 SDS of stadiometer measurements. Linear regression was used to assess correlation.

Results

Eighty-eight (46M) mean age $\pm$ SD, 9.8 $\pm$ 4.3 years (range: 1.0-17.0) patients had three consecutive GMA measurements in clinic. A significant correlation was found in height measurements obtained from GMA and stadiometer (R2 99.7%; $p<0.0001$). The average coefficient of variance for repeat GMA measurements was 0.97%. The average difference in SDS between the measurement methods was 0.26 SDS (95% CI:0.22-0.29) with 95% of GMA measurements within ± 0.5SDS of stadiometer measurements. Twenty-eight (19M) mean age $\pm$ SD, 8.8 $\pm$ 4.6 years (range: 1.0-17.0) participants had GMA home measurements, which correlated significantly (R2 99.2%; $p<0.0001$) with clinic stadiometer measurements.

Conclusion

GrowthMonitor produces accurate, reliable height measurements and can be used by parents in the community to capture serial height measurements.

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OC10.4

Increasing patient adherence and reducing drug wastage: impact of a personalised patient support programme integrated with a digital connect ecosystem

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Background
For chronic non–life-threatening conditions such as growth hormone deficiency, adherence to treatment can be difficult to maintain at a high level especially when the benefits are not immediately apparent.[1] Here, we briefly explore some of the components within an e-health ecosystem that aims at personalizing treatment and improving adherence among patients receiving recombinant human growth hormone (r hGH; somatropin, Merck Healthcare KGaA, Darmstadt, Germany)
Objective
To better understand the impact of a personalised patient support programme (MySupport[2]) embedded in a digitally connected ecosystem (Easypod® connect – EPC Next) for patient adherence and drug wastage, aggregated pseudoanonymised data (from January 2019 to December 2020) was analysed ($n=73$). In addition, three case studies were observed at baseline reflecting patients with low, medium, and high adherence, assessing also the effect of low adherence on drug wastage.[3]
Results
As a result of a combined approach of PSP interventions based on utilisation and integration of the EPC system along with close collaboration with clinical endocrinology teams, the average patient adherence to r hGH treatment over the course of 2 years was 83% ($n=73$). Focusing on 3 case studies, adherence was found to improve with an average supported adherence of 95%. Using the 2nd case study demonstrating medium adherence as an example, the cost of drug wastage reduced from €178.71 to €12.77 over one calendar month.[3]
Conclusion
With the combined support provided by the clinical teams, the MySupport PSP and the adherence monitoring capabilities of the EPC platform, patient adherence and treatment optimisation appeared to be positively impacted. EPC Next highlights when adherence support is required and provides a better measure for the success of the interventions provided by clinical and PSP teams to support dose adjustment decisions, improve adherence to treatment, and reduce drug wastage.

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OC10.5

Factors affecting the hypoglycaemic response in the insulin tolerance test in paediatric patients

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Background
The Insulin Tolerance Test (ITT) is the gold standard for assessing pituitary function in adults, but used variably in paediatrics due to concerns of serious adverse events. Our aim was to assess the safety of ITT and identify factors associated with the hypoglycaemic response.
Methods
We retrospectively collected the following data from patients who underwent ITT ($n=122$) under Paediatric Endocrinology from 2019-2021: demography, anthropometry, indication for ITT, pituitary deficiencies, insulin dose, blood glucose (BG) values, IGF1, peak growth hormone (GH) and cortisol levels, features and treatment of hypoglycaemia, and adverse outcomes. Severe biochemical hypoglycaemia (SBH) was defined as nadir BG (NBG) $\leq$2.0 mmol/l and poor response to treatment (PRT) as further decrease in BG despite glucose administration.
Results
90 patients were evaluated for GH deficiency diagnosis (age = 12.0 $\pm$ 3.0yrs) and 32 underwent re-evaluation at final height (age = 17.4 $\pm$ 1.5yrs), with mainly standard insulin dose of 0.1units/kg (2 received 0.05units/kg and 0.15units/kg each). The mean basal BG (BBG) was 4.91 $\pm$ 0.52 mmol/l, NBG 1.83 $\pm$ 0.53 mmol/l and duration of hypoglycaemia 14.1 $\pm$ 8.7 minutes. 112 (92.6%) patients achieved adequate hypoglycaemia (BG $<$2.6 mmol/l). 81 (66.9%) patients developed SBH and 65 (53.3%) PRT. None developed seizure, unconsciousness or other serious hypoglycaemia-related adverse effects. 3 (2.7%) patients received IV glucose and one IV hydrocortisone for poor oral intake/prolonged hypoglycaemia. Duration of hypoglycaemia was longer in patients assessed for re-evaluation than for diagnosis (19.0 $\pm$ 12.4 vs 12.5 $\pm$ 6.4 minutes, $P=0.001$), but NBG were similar. NBG was associated with BBG ($r=0.42$, $p<0.0001$) and peak cortisol levels ($r=0.21$, $P=0.022$), but not peak GH levels or BMI. PRT was associated with lower BBG ($r=$-0.29, $PPPP=0.002$) and peak cortisol levels ($r=$-0.20, $P=0.027$). BBG of $\leq$4.0 mmol/l (approximately $<-$2SD of BBG) was associated with higher proportion of SBH (83.3% vs 66.4%) and PRT (100% vs 53.0%). Duration of hypoglycaemia was associated positively with age ($r=0.25$, $P=0.009$) and number of pituitary deficiencies ($r=0.22$, $P=0.020$), and negatively with BBG ($r=$-0.23, $P=0.015$).
Conclusions
Despite the high incidence of SBH, there were no significant hypoglycaemia-related adverse events. Reducing insulin dose to 0.05units/kg when cortisol deficiency is likely or BBG $\leq$4.0 mmol/l and using a higher hypoglycaemia threshold may reduce the frequency of SBH and duration of hypoglycaemia.

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OC10.6

A comparative study observing the association between graves' disease and the covid-19 pandemic in children

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Background
Coronavirus 2019 (Covid-19), an infectious disease caused by SARS-CoV-2 virus has been linked to autoimmunity. Graves' disease (GD) is a common subtype of paediatric hyperthyroidism and an autoimmune condition, where antibodies stimulate the thyroid-stimulating hormone receptor on the thyroid gland to produce excess thyroid hormone. Although, paediatric GD is rare, incidence have risen before the pandemic, and this rise has accelerated since the Covid-19 pandemic.
Objectives
To compare incidence, severity, and healthcare access of newly diagnosed paediatric patients with GD before and during the pandemic.
Method
We analysed retrospective data of newly diagnosed patients between period A: October 2017-January 2020 (pre-pandemic) and period B: February 2020-May 2022 (pandemic). Data was gathered from two large Welsh centres (University Hospital of Wales and Royal Gwent Hospital) using the Paediatric Endocrinology Database and Welsh Clinical Portal. The parameters compared were age, demographic, clinical presentation, treatment, remission, and relapse.
Results
The study including 29 patients saw increased cases of GD, from 31% in period A, pre-pandemically to 69% in period B, during the pandemic. In period A, 78% patients reported familial autoimmunity, which decreased to 35% in period B. Psychological and toxic symptoms such as thyroid eye disease (TED) increased in period B. TED occurred in 1 in 9 patients in period A, compared to 1 in 5 in period B with a 9% incidence increase in period B. 1 patient had thyroid storm in period B. TPOAb levels were also higher in period B. GP and A&E referrals increased by 26% and 9% respectively in period B. In period A, patients continued one regime, titration (78%) or block and replace (22%). In period B, 32% patients changed from titration to block and replace, of which 33% had TED. 11% patients from period A relapsed during the pandemic. 5% patients diagnosed in period B achieved remission, no relapses were recorded.
Conclusion
The study showed increased incidence of GD during the pandemic suggesting possible association of Covid-19 and GD. A shift in the mode of accessing healthcare and rise in severity and prevalence of psychological symptoms were seen.

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Poster Presentations

Adrenal 1

P1

Recommendations for hydrocortisone doses for emergency management and peri-operative care for childhood adrenal insufficiency. BSPED consensus guidelines

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Adrenal insufficiency (AI) is characterised by lack of cortisol production from the adrenal glands which is treated with replacement doses of hydrocortisone. At times of physiological stress there is an increased requirement for exogenous glucocorticoids, which if untreated can lead to an adrenal crisis. Currently there are no unified guidelines for those <18 years old in the UK; this can lead to a substantial variation in the management of AI in both an emergency and peri-operative situation. The Paediatric AI Group (17 professionals from nine centres including paediatric endocrinologists, specialist nurses and a pharmacist) was set up in 2021 under the auspices of the BSPED to provide national guidance. For sick days the preferred consensus option is approximately 30 mg/m^2/day hydrocortisone given as 4 equally divided doses for moderate to severe illness. This allows accuracy of dosing at regular 6 hourly intervals. In acute situations the emergency dose of intramuscular hydrocortisone is 25 mg <1 year, 50 mg 1 to 5 years and 100 mg ≥ 6 years, followed by 2 mg/kg (max 100 mg) (neonates 4 mg/kg) IV initially 4 to 6 hourly, then reduced to 1 mg/kg (max 50 mg) (neonates 2 mg/kg) IV 6 hourly when stable before switching to oral sick day hydrocortisone. For surgical procedures a bolus of hydrocortisone 2 mg/kg (neonates 4 mg/kg) (max 100 mg) is required at induction for general anaesthetic. This is followed by either a) a hydrocortisone infusion based on the weight of the child (<10 kg 25 mg in 24 hours; 10.1 to 20 kg 50 mg in 24 hours; 20.1 to 40 kg 100 mg in 24 hours, 40.1 to 70 kg 150 mg in 24 hours, over 70 kg 200 mg in 24 hours) or b) hydrocortisone IV boluses 1 mg/kg (neonates 2 mg/kg) (max 50 mg) every 6 hours. If required, during prolonged operations or if unstable, the initial bolus dose can be repeated at a 4 to 6 hour intervals. In severe obesity 100 mg of hydrocortisone can be given every 6 hours. The broad management principles from this group will be used to create documents on sick day steroid recommendations, standardised surgery advice, a new BSPED emergency card, a publication, on-going training and education and engagement with support groups and professional societies.

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P2

Salivary adrenal biomarkers differ depending on age and sex in healthy children: preliminary data

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Background
Saliva is ideal for measuring free, biologically active hormones. Measurements of salivary androgens may be valuable in diagnosis and monitoring of adrenal disorders, however the diurnal profile and robust reference ranges in healthy children are currently undefined. We report salivary testosterone, androstenedione (A4), 11-ketotestosterone (11-KT), 11-β hydroxyandrostenedione (11β-OHA4) concentrations measured throughout the day in healthy children.
Methods
Participants provided salivary samples using Salivettes (Salimetrics®) 30 minutes after waking and 2-hourly thereafter. Participants did not eat or brush their teeth prior to sampling. Children with a family history of inherited adrenal disorders, oral lesions or conditions/medications likely to affect cortisol concentrations were excluded. Pubertal examinations were not performed to optimise recruitment. An age of nine in girls and ten in boys was used to define pre-puberty and puberty. Samples were analysed by LC-MS/MS.
Results
54 (30M) healthy children, aged 10.4 $\pm$ 3.9 (5.0-17.5) years participated. Body mass index standard deviation score was 0.4 $\pm$ 1.1. All hormones showed a circadian rhythm, with a steep decline between measurements made 30 minutes and 2 hours after waking. Area under the curve (AUC) for testosterone, A4, 11-KT and 11β-OHA4 are given below.
Conclusion
To our knowledge, this is the first description of the circadian profile of salivary androgens, and age and sex differences, in healthy children. Testosterone was higher in boys than in girls, the converse was true for other androgens. The significant differences between sex, and age groups indicate that larger data sets are required to define reference data for children.

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P3

Mean glucose concentrations are increased, and cardiovascular risk factors are common in children and young people with secondary adrenal insufficiency (GRACE2)

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Background
Hypoglycaemia, possibly due to non-physiological hormone replacement, and poor cardiovascular outcomes are described in patients with adrenal insufficiency (AI), particularly in the adult population. In this study, we describe glucose profiles and risk factors for premature cardiovascular disease (CVD) in children with secondary AI (SAI).
Methods
Participants underwent continuous glucose monitoring (CGM), for seven days (blinded Dexcom G6 monitor). The following risk factors for CVD were measured: clinic blood pressure (BP) and 24-hour ambulatory BP monitoring (ABPM), carotid intima media thickness (CIMT), brachial artery flow mediated dilatation (FMD), body mass index standard deviation score (BMI SDS), HOMA-

Hormone	Mean area under the curve (95%CI)						
	Prepubertal			Pubertal			
	Girls, $n=12$	Boys, $n=14$	*P*-value	Girls, $n=12$	Boys, $n=16$	*P*-value	*P*-value
Testosterone	321.8	357.3	<0.0001	573.2	859.5	<0.0001	
(pmol/l)	(215.8-427.8)	(265.7-448.9)a		(363.8-782.6)	(443.1-1276.0)		
	343.2 (248.6-437.8)			741.0 (389.5-1094.0)			<0.0001
A4	1953.0	1478.0	<0.0001	1675.0	1332.0	<0.0001	
(pmol/l)	(1178.0-2728.0)	(891.0-2057.0)		(978.8-2372.0)	(917.8-1746.0)		
	1688.0 (1005.0-2371.0)			1259.0 (741.8-1775.0)			<0.0001
11-KT	459.4	383.0	0.0001	1304.0	1209.0	0.0271	
(pmol/l)	(190.2-728.5)	(234.5-531.5)b		(833.2-1775.0)a	(638.0-1779.0)a		
	424.1 (205.5-642.8)			1259 (741.8-1775.0)			<0.0001
11β-OHA4	1285.0	929.1	<0.0001	1546.0	732.3	<0.0001	
(pmol/l)	(478.9-2092.0)	(495.7-1363.0)b		(814.5-2277.0)a	(456.2-1008.0)a		
	1106 (462.0-1751.0)			1131 (539.3-1722.0)			0.4867

a $n=13$, b $n=12$

IR [(fasting insulin (microU/l) x fasting glucose (nmol/l)/22.5)], and von Willebrand factor (vWF) antigen and activity.
Results
20 (9M) patients, median age 13.0 years (IQR 9.8-15.3), 6 congenital and 14 acquired SAI participated. All had ≥1 other hypothalamic-pituitary axis affected. Hydrocortisone dose was 8.6 ± 1.4 mg/m^2/day, height SDS -0.2 ±1.25, BMI SDS 1.8 ±1.5. Mean glucose levels were higher in SAI than in data reported in healthy children 5.91 (± 0.43) mmol/l vs 5.55 (± 0.36) mmol/l, $P<0.001$[1]. Risk factors for CVD are shown below.
Conclusion
To our knowledge, this is the first report of elevated glucose concentrations in patients with SAI, the clinical significance of which is unknown. It is possible that minor, but lifelong increases in blood glucose have an adverse effect on health. We identified multiple risk factors for CVD, and early intervention to address modifiable risk factors may improve long term cardiovascular health.
References
1. Shah, V.N., *et al* (2019) *JCEM*

Cardiovascular risk factors in children with secondary adrenal insufficiency

	Mean (±SD)	Number (%) >95th centile
Cardiovascular outcome		
Clinic BP		
• Systolic percentile	67.9 ± 20.2	1 (5.0%)
• Diastolic percentile	60.8 ± 29.8	2 (10.0%)
ABPM		
• Systolic percentile		0 (0.0%)
• Diastolic percentile		1 (5.0%)
• Loss of nocturnal dip*		8 (57.0%)
CIMT (mm)	0.43 ± 0.03	4 (22.2%)
FMD (%)	10.6 ± 6.3	3 (20.0%) **
Metabolic outcome		
BMI SDS	1.8 ± 1.49	11 (55.0%)
HOMA-IR (mass units)	5.0 ± 6.15	7 (38.9%)
VWF antigen and activity (%)	-	4 (28.6%)

*less than 10% difference in day and night readings **Measurements <7%, reference range 7-15%

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P4

Establishing the utility of the 60-minute serum cortisol sample in a standard synacthen test in a tertiary paediatric centre

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Background
The standard synacthen test (SST) is commonly utilised to interrogate the hypothalamo-pituitary-adrenal (HPA) axis in children. It comprises baseline and 30-minute serum cortisol concentrations (SCC), after injecting synthetic adrenocorticotropic hormone (ACTH)[1–24]. There is debate regarding the utility of a 60-minute SCC in the SST protocol with most studies to date conducted in adults.
Aim
To assess the utility of a 60-minute SCC in the SST to diagnose adrenal insufficiency (AI) in children.
Method
A retrospective, single-centre study was conducted at a tertiary paediatric hospital. Anonymised data from April 2019-November 2021 was analysed. Both 2-sample SST (baseline and 30-minute SCC), and 3-sample SST (baseline, 30- and 60-minute SCC) were conducted during this period due to local protocol variation. SCC was measured by immunoassay (Siemens IMMULITE-2000XPI analyser).
Results
Data from 160 patients was analysed (mean age 6.3years [0.0008-24.9]; 86 female). 54% were steroid naïve. 93 patients underwent a 2-sample SST and 67 underwent a 3-sample SST. There was a positive correlation between 30- and 60-minute SCC ($r=0.96$, $P< 0.001$) and no patient with a 30-minute "optimal" response (SCC >500nmol/l) had a "sub-optimal" response (SCC <500nmol/l) at 60 minutes. 52% ($n=83$) had a sub-optimal response at 30 mins and the baseline SCC was not predictive of this. 13.4% of those who achieved a SCC>500nmol/l at 60 minutes were classified as a "delayed pass" (SCC <500nmol/l at 30-minutes).
Conclusion
Results from this paediatric cohort suggest there is utility in the inclusion of 0-, 30-, and 60-minute SCC as part of the SST. The 30-minute SCC measurements have been validated against the gold-standard insulin tolerance test, however relying on this alone may over-diagnose AI, resulting in unnecessary regular treatment with exogenous steroid. The SCC at 30 minutes, produced in response to synacthen stimulation, is an indicator of the readily releasable pool of cortisol. The SCC at 60 minute is indicative of cortisol synthesis, dependent on ACTH signalling. Relying on a 60-minute SCC alone may result in a diagnosis of a "normal" HPA axis, when in fact glucocorticoid support during sickness/stress may be prudent if the 30-minute SCC is found to be sub-optimal.

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P5

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P6

Partial CYP11A1 deficiency presenting with childhood hypoglycaemia

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Case
A previously well 2.5 old boy with a height and weight on the 50th centile presented to his local Emergency Department with pyrexia, vomiting, and a history of poor appetite. His parents were consanguineous and of Turkish ancestry. Blood glucose level on arrival was 1.9 mmol/l and there was evidence of mild metabolic acidosis. Investigations at the end 19 hour controlled fast demonstrated a normal ketotic and free fatty acid response with adequately suppressed insulin. Peak growth hormone and cortisol response to a glucagon stimulation test was 8.2 mg/l and 194nmol/l respectively. The child was discharged with a diagnosis of ketotic hypoglycaemia and a sickness emergency plan. By the age of 3 years, he had had two further similar episodes of hypoglycaemia and vomiting. He was referred to a tertiary centre at the age of 4 years for further investigation. Investigations demonstrated an ACTH concentration of 519ng/l, an AM cortisol of 188nmol/l, normal electrolytes, normal 17-hydroxyprogesterone and a normal urine steroid profile. A low-dose Synacthen demonstrated a peak cortisol response of 301nmol/l and a two hourly cortisol profile revealed a low mean cortisol concentration of 104nmol/l. A diagnosis of primary adrenal insufficiency (PAI) was made and the child commenced on maintenance hydrocortisone of 10 mg/m^2/day. Research exome sequencing was conducted and found a homozygous missense mutation in *CYP11A1* (R451W) which is predicted in silico benign. However, this variant has been shown to cause partial *CYP11A1* deficiency and resultant PAI through missplicing. Furthermore, the variant arises from a 'hotspot' within central Turkey.
Discussion
Partial *CYP11A1* deficiency is associated in two thirds of cases with concomitant aldosterone deficiency and more recently is associated with an infertility reproductive phenotype. This case emphasises the value of a genetic diagnosis in PAI and the influence of genetic 'founder effects'.

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Bone

P7

Does maternal deprivation have a bearing on the newborn vitamin D status?

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Objectives
Examine the effect of maternal Index of Multiple Deprivation (IMD) on newborn 25-hydroxyvitaminD (25OHD) levels in a multi-ethnic newborn cohort.
Design
3000 dried blood spots (DBS) were gathered from newborns at a regional newborn screening laboratory over two 1-week periods [February 2019 (winter) and August 2019 (summer)]. Data on birth weight, gestational age, maternal age, ethnicity, and post code were collected. Post code was replaced with lower layer super output area (LSOA). IMD quintiles for the corresponding LSOA was used to ascertain socio-economic status (SES) [quintile one (Q1) representing the most deprived 20% and quintile five (Q5) the least deprived 20% of the population]. Each of the seven domains of IMD were examined (income, employment, education, health, barriers to housing and services, crime and living environment). 25OHD was measured on 6mm sub-punch from DBS using quantitative liquid chromatography tandem mass spectrometry and equivalent plasma values derived.
Results
A total of 2999 (1500 summer-born, 1499 winter-born) newborn DBS (1580 males) were analysed. 35.7% were vitamin D deficient [25OHD < 30 nmol/l] and 33.7% insufficient [25OHD 30-50 nmol/l]. Summer-born newborns had significantly higher 25OHD concentrations compared to winter-born [49.2 vs 29.1 nmol/l respectively, $P<0.001$]. 25OHD levels varied significantly between the IMD quintiles in the whole ($P<0.001$) and summer-born cohort ($P<0.001$), but not in the winter-born cohort ($P=0.26$), whereby the most deprived cohort had the lowest 25OHD concentrations. Among the seven independent domains of deprivation, living environment had a significant influence on 25OHD levels ($\beta=0.07$, $P=0.002$). In this subdomain, mean 25OHD levels varied significantly between quintiles in the whole ($P<0.001$) and in the summer-born cohort (Q1 46.45 nmol/l, Q5 54.54 nmol/l; $P<0.001$) but not in the winter-born cohort (mean Q1 31.57 nmol/l, Q5 31.72 nmol/l; $P=0.16$). In a regression model, living environment was still significant ($P=0.018$) and season of birth and ethnicity had a greater effect on 25OHD levels.
Conclusion
Maternal living environment has the greatest influence on newborn 25OHD levels among the seven domains of deprivation. Enhanced supplementation and food fortification have been shown to overcome the above non-modifiable risk factors and should be seriously considered.

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P8

Burden of disease in family members of children presenting with symptomatic vitamin D deficiency: who to test and when?

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Background
The extent of biochemical abnormalities in household members of children presenting with symptomatic vitamin D deficiency remains unknown. Characterising risk groups who warrant 25 hydroxyvitamin D (25OHD) testing will help reduce the rising frequency of unnecessary testing in the UK.
Aims
Investigate the prevalence of vitamin D deficiency and biochemical osteomalacia in the mothers and siblings of children presenting with symptomatic vitamin D deficiency. Identify risk factors for severe deficiency in family members.
Methods
All mothers and sibling of children referred to a single tertiary endocrine centre between January 2018 and December 2021, with symptomatic vitamin D deficiency were investigated prospectively for vitamin D deficiency [defined as 25OHD < 30nmol/l] and biochemical osteomalacia [vitamin D deficiency and elevated alkaline phosphatase (ALP) and/or parathormone (PTH)] as per clinical guidelines.
Results
Ninety-seven family members (68 siblings and 29 mothers) of 29 index cases (median age 1.7 years, 55.5% male) were investigated. The majority (65.5%, $n=19$) were of Asian ethnic background. The mean (SD) 25OHD levels of the index, maternal and sibling cohorts were 15 (10), 15 (7) and 20 (10) nmol/l respectively. Vitamin D deficiency was noted in 93% of the maternal and 79% of the sibling cohorts. Biochemical osteomalacia was present in 72% of the maternal and 79% of the sibling cohorts. Mothers of infants had significantly lower mean 25OHD levels compared to mothers of older children [11 ($n=12$) vs 18 nmol/l ($n=17$) respectively, $P=0.006$)], most of whom were symptomatic (66.6%, $n=8/12$). Among the 10% ($n=7$) of the siblings with hypocalcaemia, 86% ($n=6/7$) had concurrent dietary calcium deficiency and 71.4% ($n=5/7$) reported symptoms in retrospect. Hypocalcaemic siblings had significantly lower 25OHD (7 vs 15 nmol/l, $P<0.001$), higher PTH (175 vs 58 ng/l, $P<0.001$) and ALP (846 vs 318 IU/l, $P<0.001$), respectively compared to normocalcaemic siblings.
Conclusions
We recommend universal vitamin D supplementation of all family members of children diagnosed with symptomatic vitamin D deficiency. Biochemical testing is indicated in those at highest risk such as mothers of infants, individuals with concurrent dietary calcium deficiency and those with clinical symptoms.

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P9

Bone biochemistry in children with fractures presenting with non-accidental injury

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Background
Fractures are reported in 1/3 of children who have been abused. The Royal College of Paediatrics and Child Health (RCPCH) recommends that assessment of fractures where there is suspicion of physical abuse should include bone biochemistry: calcium (Ca), phosphate (Ph), alkaline phosphatase (ALP), parathyroid hormone (PTH) and Vitamin D (VitD).
Objectives
To describe the pattern of bone biochemistry in children with fractures when non-accidental injury (NAI) is suspected.
Methods
A retrospective review of case notes, electronic results database, and radiology records over a ten-year period (2012- 2021) at the Royal Hospital for Children, Glasgow (RHCG). Children who were under two years of age who had undergone a skeletal survey as part of a child protection investigation where one or more fractures were identified were included. Established criteria to classify NAI were used to distinguish confirmed NAI from non-NAI. Bone biochemical markers were classified as normal or abnormal using local reference ranges. VitD deficiency was classified as VitD <25nmol/l and insufficiency as 25-50nmol/l.
Results
One hundred and twenty children were identified, of whom 107 (89.2%) had bone biochemistry performed. Twenty-nine children (24.2%) had injuries that were classified as confirmed NAI. The remainder were classified as highly suspicious of NAI ($n=7$,5.8%), suspicious of NAI ($n=14$,11.7%), unexplained ($n=16$,13.3%) and accidental ($n=54$,45%). Forty-three (40.2%) children[am1] were identified as having either one or more abnormal bone biochemical markers. One child was found to be vitD deficient, a further 27/107 (25%) were found to be insufficient. In cases where NAI was confirmed either at case conference or by criminal conviction 14/29 (48.3[am2] %) had one or more abnormal bone biochemical markers. None of the children displayed clinical or radiological evidence of rickets.
Conclusion
Children undergoing investigation of a fracture in suspected NAI often have a vitD in the deficient or insufficient range in the absence of clinical, radiological, or biochemical evidence of rickets. Other bone biochemical markers are frequently outside the normal reference ranges in this population.

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P10

Hypophosphatemic rickets as a key presenting feature of tyrosinemia type 1

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Tyrosinemia type-1 is a rare autosomal recessive disorder. It usually presents in an acute form in early infancy. Rarely, it can also present as a chronic form with gradual onset. The key presenting features are failure to thrive, liver dysfunction and/or Fanconi syndrome. We present a perplexing case of a 2-year-old girl with tyrosinemia type-1, who initially presented with failure to thrive and hypophosphatemic rickets without overt liver dysfunction and required extensive input from oncology, endocrinology, liver, renal and metabolic teams before diagnosis was established. She had an elevated fibroblast growth factor 23 (FGF23) level, which is unexpected as FGF23 would normally be low in Fanconi hypophosphatemia.
Presentation
A 2-year-old girl was acutely referred by her health visitor due to concerns of poor appetite, tiredness, faltering growth, loss of ability to walk independently and progressive bowing of legs discovered during her routine 2-year check.
Examination
Height: 74.1 cm (<0.4th percentile), weight: 8.5 kg (0.4th percentile), bowed legs, rachitic rosary and mild hepatomegaly
Investigations
Urea and electrolytes: normal, Suspected diagnosis: oncogenic osteomalacia Further investigations: MRI abdomen: numerous T2 hypointense lesions, no features of hepatoblastoma/hepatocellular carcinoma Plasma tyrosine level: 533 umol/l (38–160) Urine: increased excretion of succinyl acetone and generalised aminoaciduria Liver biopsy: advanced fibrosis Final diagnosis: tyrosinemia type-1 Treatment: nitisinone, protein restriction, phosphate and calcium supplements and alfacalcidol Currently, she is 10 months post-diagnosis and is again walking independently. FGF23 is high at 128 RU/ml and urine phosphate is still elevated at 33 mmol/l.
Conclusion
FGF23 may have a role in the causation of hypophosphatemia in patients with tyrosinemia, and this merits further investigation.

Alkaline Phosphatase	1876 U/l
Phosphate	0.23 mmol/l
Adjusted Calcium	2.22 mmol/l
Vitamin D	91 nmol/l
Parathyroid Hormone	183 ng/l
Alanine Aminotransferase	30 U/l
PT	15.8
APTT	37.0
Bicarbonate	14 mmol/l
Chloride	109 mmol/l
X-ray Wrist	Rickets
Ultrasound	Hepatomegaly with innumerable scattered nodules and enlarged kidneys

Alpha Fetoprotein	14398 kU/l
Zinc Protoporphyrin	>600 umol/mol
FGF23	209 RU/ml (0–100)
Urinary Phosphate	62.6 mmol/l
Urine Ca:Cr ratio	1.45 mmol/mol

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P11

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P12

A case series of 8 patients with pseudohypoparathyroidism and variable phenotype

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Introduction
Pseudohypoparathyroidism (PHP) is a group of heterogeneous disorders causing parathyroid hormone (PTH) resistance. The features could include Albright's hereditary osteodystrophy phenotype (AHO) [brachydactyly, short stature, obesity, round face, ectopic ossifications, intellectual disability]. The condition is rare with an estimated prevalence of 0.34-1.1 in 100,000 and the clinical presentation can be variable. Herein, we present 8 patients with PHP from two centres (Alder Hey Children's Hospital, UK and Endocrine Research Centre, Russia) with a wide variation in the clinical presentation.
Patients and methods
PTH resistance was established by the presence of high PTH with low/normal plasma calcium, high/normal plasma phosphate, and normal vitamin D. *GNAS* genetic testing was undertaken in 7/8 cases and positive in 5 patients.
Results
5 girls and 3 boys with PHP were included. Five patients had PTH resistance and AHO (type 1a), two had only biochemical abnormalities (type 1b), and one had AHO and borderline laboratory results. Median age at presentationwas4 years (range 6 months - 14 years). Patients were referred with a range of symptoms: seizures, excessive weight gain and subcutaneous ossifications. Most patients (6/8) had hypocalcaemia and hyperphosphatemia. Interestingly, one of these children had temporary normalisation of calcium, phosphate and PTH levels. Two patients always had normal calcium and phosphate levels. TSH resistance was found in 7/8 cases. The features of AHO phenotype identified include brachydactyly (6/8), learning difficulty (6/8), round face (5/8), ectopic ossifications (3/8), overweight (3/8), and short stature (1/8). We also noted some uncommon features in our group, such as tall stature and advanced bone age. One child presented with medulloblastoma. 6/8 patients were treated with Alfacalcidol (0.6 - 8 mg/day).
Conclusion
Patients with PHP have heterogenous clinical and biochemical picture. Among phenotypical changes, brachydactyly, learning difficulties, and round face are most common ones in our group. Laboratory results can reveal normal calcium and phosphate levels in some patients. Due to overlapping symptoms, new classification of inactivating PTH/PTHrP signaling disorders might be beneficial.

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P13

Atypical persistence of neuropsychiatric symptoms in adolescents with primary hyperparathyroidism post parathyroidectomy- a review of two cases

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Introduction
Neuropsychiatric manifestations are well recognised in patients with primary hyperparathyroidism (PHP). Abnormal calcium channel physiology has been implicated in several pain disorders. The psychopathology emerges after prolonged subclinical hypercalcemia, but there is poor correlation with symptom severity. We report the complex management of two adolescents with PHP, secondary to parathyroid adenoma (no predisposing germline mutation identified), with persistent symptoms following successful parathyroidectomy.
Case Report
Case 1: 15-year-old boy, with a background of attention deficit hyperactivity disorder, Tourette's syndrome and oppositional defiant disorder, who presented with paraesthesia and numbness. He had severe hypercalcaemia, requiring urgent parathyroidectomy and since maintained normal biochemistry. In the early post-operative period, he developed numbness in his arms, chest tightness, headaches and blurred vision. Investigations including bone profile, vitamin D, MRI brain and spine were normal. He continues to have lower limb pain and is now jointly managed with CAMHS and pain clinic. However, he described a significant improvement in symptoms after starting antidepressant (Fluoxetine) and ADHD medication (Lisdexamfetamine). Case 2: 15-year-old-girl presented with lethargy, low mood, bone pain, anorexia, weight loss, hair thinning and polydipsia. Blood tests, ultrasound and Tc-99m-sestamibi scans revealed a right lower parathyroid adenoma. She was started on Cinacalcet with no improvement in symptoms. Her biochemistry normalised following parathyroidectomy. However, post-operatively, her lethargy, bone pain, low mood, weight loss and poor appetite persisted for over 9 months. After a normal Rheumatology assessment, she is now followed up at the chronic fatigue clinic.
Discussion
We describe two adolescents with normal biochemistry following successful parathyroidectomy for PHP, secondary to parathyroid adenoma, that report ongoing symptoms – beyond the time within which resolution would be expected. Neuropsychiatric symptoms can be a presenting feature of hypercalcaemia; however, the mechanism remains poorly understood. Resolution is expected soon after parathyroidectomy and reports of persistent symptoms are rare. Could

prolonged hypercalcaemia cause permanent neurological dysfunction? Further studies are needed to better understand the aetiology and post-operative course of neuropsychiatric symptoms due to PHP. A multidisciplinary approach is essential in managing the medical, surgical and mental health challenges this condition can present with.

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P14

A novel GNAS variant in a child with hyperphagia, obesity, brachydactyly and normocalcaemia

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Introduction
Pseudohypoparathyroidism type 1A (PHP1A) is a rare genetic disease characterized by resistance to parathyroid hormone along with hormonal resistance and features of Albright hereditary osteodystrophy (AHO). This is caused by heterozygous inactivating mutations in the maternal allele of the GNAS gene, which encodes the stimulatory G-protein alpha subunit (Gsα) and regulates production of second messenger cyclic AMP. Here, we report a previously undescribed GNAS variant in a child with hyperphagia, obesity, mild brachydactyly and normocalcaemia.
Case
A 6-year-old female presented with hyperphagia and significant weight gain from 3 years of age. Her weight was 47.1 kg (3.72 SDS), BMI 30.39 (4.05 SDS) with height (1.89 SDS) and HC 56 cm (3.01 SDS). She had brachydactyly with short fourth and fifth metacarpals, short toes and a café au lait patch on the chest. Birth weight was 3.79 kg (1.12 SDS). Developmental milestones including cognitive achievements were delayed. Parents were non-consanguineous; her older brother had a similar phenotype with hyperphagia.
Results
PTH was slightly high [9.5 pmol/l (0.7-5.6)] with normal calcium and Vitamin D, TSH 6.6 mU/l (<6), T3 10.3 pmol/l (6.2-9.5), FT4 11.8 pmol/l (10.8 - 19.0) and raised triglycerides. Ultrasound abdomen revealed mild diffuse fatty liver. X-ray hand showed generalised mild brachydactyly with short right fifth metacarpal. Next Generation Sequencing (NGS) of the coding region of the genes in the Obesity gene panel detected a novel heterozygous (c.791A>C, p.(Asn264Thr) mutation in the GNAS gene. This mutation was also identified in her mother and brother confirming maternal inheritance of the familial GNAS variant. This variant has not been reported in control databases (1000 Genomes, ESP, ExAC and gnomAD, Human Gene Mutation Database and ClinVar) and has been classified as pathogenic using ACMG and ACGS guidelines.
Discussion
In conclusion, the novel heterozygous GNAS variant c.791A>C, p.(Asn264Thr) results in altered Gsα function, which furthers our understanding of the pathogenesis of this disease. Screening for GNAS mutations should be considered in suspected cases of PHP1A even if the classical signs are not present. The obesity gene panel is able to detect GNAS variants as a cause of obesity.

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Diabetes 1

P15

Blindness at initial presentation of new onset diabetes mellitus in a 13 year old girl

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Background
Bilateral cataracts are rarely the initial symptom of diabetes mellitus (DM). Patients with DM who developed cataracts usually have DM for many years. The prevalence of early cataracts in paediatric DM ranges between 0.7 and 3.4%. We report a case of DM diagnosis following onset of blindness due to new bilateral cataracts.
Case description
13-year-old Caucasian girl presented with rapidly declining vision for 2 months. She was blind 2 weeks prior to presentation. Examination showed significant posterior subcapsular cataracts and visual acuity of 1/60 bilaterally. Urgent cataract surgery was scheduled. 3 days before surgery, she attended emergency department with HbA1c of >146 mmol/mol and polydipsia for 7 weeks. Blood glucose was 27.8 mmol/l; ketone was raised at 1.9 mmol/l but she was not in diabetic ketoacidosis. She had no dysmorphic features and no acanthosis nigricans. Her BMI was 26.1. Anti-GAD, anti-IA2, and anti-ZnT8 were negative. C-peptide level was high at 813 pmol/l. There is family history of type 2 diabetes (T2D). Results of her genetic testing for monogenic diabetes were normal. Child had cataract surgery with lens implant in two stages and her vision improved significantly.
Discussion
The aetiology of early cataract in children with diabetes is unknown. Several theories include osmotic damage to lens structure, polyol pathway and oxidative stress. It is currently unclear what type of diabetes our patient has. Though she was ketotic on presentation, the negative autoantibody profile suggests she may not have Type 1 diabetes. T2D is a possibility given her high HBA1c, family history and raised BMI. Monogenic diabetes is not typically associated with cataracts. HNF1B (MODY5) mutation was recently linked with bilateral cataracts. In 2 other cases, patients with bilateral cataracts and negative autoantibodies had PRRC2A gene mutation and a de novo INS gene mutation.
Conclusion
New onset bilateral cataracts are rare in children and should raise suspicion of DM or other metabolic conditions.

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P16

Generic standard operating procedure (SOP) for insulin dose adjustment

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Introduction
Across the North West England, following a survey across all Children and Young People's Diabetes Units, a large number of paediatric diabetes specialist nurses (PDSNs) adjust insulin doses of children and young people with diabetes without a non-medical prescribing qualification (NMP). The majority have no Standard Operating Procedure (SOP) in place, which is essential for their indemnity. In the meantime, PDSNs who were waiting to commence the NMP (v300) course could utilise the SOP.
Objectives
To ensure that all nurses practising in children and young people's diabetes without a NMP, have a local SOP in place.
Methods
A working group comprising the Network Manager, a Paediatric Diabetes Advanced Specialist Practitioner and the two Network Lead PDSNs was created. The group worked from an SOP originally designed by the Advanced Specialist Practitioner. The draft version was shared across all of the PDSNs within the Children and Young People's North West Diabetes Network for peer review and amendments made accordingly. The final version was endorsed by the Network's Steering Group.
Results
Following a survey on the awareness and implementation of the SOP across 20 paediatric diabetes units and the results are as follows:
Diabetes Nurses now have clear prescribing boundaries:
- Age: 2-18 years
- an allowance of 10% dose adjustment of current prescription;
- exclusion criteria:
- out of expertise of the PDSN;
- parents and carers who specifically request a team member with prescribing qualifications.

Conclusions
By designing a generic Insulin Dose Adjustment SOP, all teams can utilise the SOP and adapt accordingly for local ratification processes by the individual Trust's/organisation's Medicines Management Group. PDSNs across the Network who have a ratified SOP now have indemnity to adjust insulin doses safely within structured boundaries. Further advantages include records of competencies and Trust/organisation oversight of nurses adjusting doses. The SOP has been shared nationally and is recognised as an official document by the National Children and Young People's Network, which can be accessed via the Network's website.

Responses	With NMP Qualification	Without NMP Qualification using SOP
70% (14/20)	53% (33)	47% (30)

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P17

Is there an increased incidence of type 1 diabetes in correlation with SARS- COVID 19 infection?- an east of england network survey

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Background
Recent studies have reported a correlation between the increase in incidence of Type 1 Diabetes (T1DM) in children and young people (CYP) and SARS-COVID19 Infection.
Aims and objectives
To study if there is an increase in TIDM incidence in CYP (aged 0-18yrs) post-covid19 (April 2020- March 2021) in East of England (EOE) region compared to previous years (April 2018- March 2020). To identify a correlation between T1DM incidence and the UK COVID19 incidence pattern.
Method
Survey of T1DM monthly incidence across all paediatric diabetes units (PDU) in EOE. Analysis performed using Excel graphs and Kruskal- Wallis test using SPSS software.
Results
All 17 PDU across EOE responded (100% response rate). There was an increase in T1DM incidence across EOE in 2020-2021 (429 cases) compared to 2018-2019 (333 cases) and 2019-2020 (382 cases). This increase in T1DM incidence is significant year on year when comparing 3 years (Kruskal Wallis $P=0.0143$). However the increase in T1DM incidence pre-COVID19 compared to post-COVID19 is not significant (Kruskal-Wallis 2019/20 vs 2020/21 $P=0.245$). The T1DM peak incidence across EOE was seen in June to August 2020, December 2020 to March 2021. This appears to be 3 to 4 months after the UK COVID19 waves in April 2020 (wave 1) and October 2020 to January 21 (wave 2). The seasonal viral infections were disrupted in 2020-2021 due to dominance of COVID19. The pattern of monthly TIDM incidence seen in 2020-2021 across EOE is different compared to previous years.
Conclusion
There is an increase in T1DM incidence in 2020-2021, which is not significant compared to the pre-COVID 2019-2020 year. This corresponds with the natural annual increase in TIDM incidence in CYP. The peak monthly TIDM incidence across EOE appears to be 3-4 months post-UK covid19 waves and is different to the pattern from previous years which suggests a possible correlation between the TIDM incidence and COVID 19 infections. However from this survey, a causal relationship cannot be established especially given the complex multifactorial aetiology of T1DM and more research is required.

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P18

Type 2 diabetes mellitus in children and young people; Single UK paediatric diabetes centre experience

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Background
Type 2 diabetes mellitus (T2DM) is becoming increasingly prevalent in children and young people (CYP), mainly linked to the rise in obesity. It is associated with higher and earlier risk of developing complications; therefore, prompt diagnosis and management involving the multidisciplinary team (MDT) is crucial. The aim of our study was to evaluate the current practice for T2DM management and monitoring of complications at our centre.
Methods
We performed a retrospective audit at the paediatric diabetes unit of Oxford Children's Hospital, UK. All CYP (less than 18 years) diagnosed with T2DM between 2016 and 2022 were included. We collected data related to diagnostic approach, management and follow up of this population.
Results
21 CYP aged between 9 and 18 years were managed for T2DM. There was equal distribution between both sexes (11 males, 10 females); however, most were from ethnic minority backgrounds (67% vs 33% Caucasian). Most children had a BMI over 25 at diagnosis and 12 months (86% and 70% respectively), and a third had a BMI > 35 (29% and 25% respectively). 90% of our population had an HbA1c > 53 mmol/mol at diagnosis, dropping to 35% at 12 months. Initial pharmacologic therapy consisted mainly of Metformin alone (43%), but basal bolus insulin (14%), Metformin and long-acting basal insulin (29%), fixed rate intravenous insulin infusion (9%) and Gliclazide (5%) were used. Metabolic complications noted at diagnosis included: hypertension (19%), hypercholesterolaemia (29%), hypertriglyceridaemia (38%) and deranged liver function (38%). According to 2-year post-diagnosis clinic review, only 10% had BMI <25 and 9% came off pharmacologic treatment. Although 44% managed to lower HbA1C below 48 mmol/mol, 19% HbA1C remained dangerously high (> 70 mmol/mol). We also noted significant association with syndromic obesity (24%) and learning difficulties (19%) in our cohort.
Conclusion
We observed that whilst intensive pharmacologic therapy was associated with a fall in HbA1c at 12 months, we did not see a noticeable drop in BMI which leaves this population vulnerable for further metabolic complications. Hence, we propose MDT approach including intensive dietetic involvement from diagnosis and if needed, escalation of pharmacological treatment within first 6 months to achieve better glycaemic control.

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P19

An unanticipated complication following diabetic ketoacidosis treatment

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A 12 year old male presented to the Emergency Department in severe diabetic ketoacidosis (DKA) with a new diagnosis type 1 diabetes mellitus. He had tested positive for Covid a few weeks prior resulting in a reduced appetite and weight loss. He had no other past medical history. He was treated as per the BSPED guideline for DKA and remained on the protocol for 24 hours. He had normal electrolytes on admission but DKA resolution was complicated by hyperchloraemic acidosis, mild hypernatraemia and mild hypokalaemia. Hours after completing his DKA treatment, having commenced subcutaneous insulin and normal oral intake, he developed severe hypokalaemia (2.0 mmol/l) and moderate hypophosphataemia (0.66 mmol/l). Despite electrolyte replacement, both his potassium and phosphate levels kept falling. On review of his history, he was a competitive boxer with regular weigh-ins and over the preceding four weeks his weight had plummeted from 48 kg to 35 kg on admission, a loss of 27% of his body weight. His electrolyte imbalances were secondary to refeeding syndrome in view of his prolonged period of reduced intake followed by a rapid return in his appetite. However, this diagnosis was not considered initially until further history taking was carried out. Fortunately, after 48 hours of ongoing replacement, his electrolytes stabilised with no evidence of organ dysfunction. ASPEN defines Refeeding syndrome as a reduction in phosphorous, potassium and/or magnesium by >10%, and/or organ dysfunction as a result of electrolyte decrease or from thiamine deficiency, occurring within 5 days of the reintroduction of calories (1). This case demonstrates the importance of a thorough history, particularly when a patient's recovery does not progress as expected. Moreover, it highlights the importance of considering the risk of refeeding syndrome for all children who have not received optimal nutritional support for >3 days (2), a common occurrence in children newly diagnosed with type 1 DM, whether they present in DKA or not. Early recognition facilitates appropriate electrolyte management, controlled refeeding and timely initiation of thiamine supplementation.

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P20

A review of our diabetes transition service: clinic attendance, average HbA1c and hospital admissions in patients between the ages of 15 to 21 years old

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Background
The move from paediatric to adult services comes at a time in a young person's life when they face multiple life challenges alongside managing their diabetes. Despite our NHS trust having a planned and integrated diabetes transition service, as per NICE (2016) and NHS England (2016) recommendations, we noticed a rise in patient's not attending clinic and suboptimal glycaemic control.

Aim
To review the data on clinic appointments attended, DNA rates, HbA1c and any hospital admissions in our transition age group from 15 to 21 years old.
Method
We reviewed data on all patients who attended transition clinics at our University Hospital between 2011 and 2019. We categorised the age ranges to 15-17 years, 17-19 years and 19-21 years old. We calculated mean HbA1c values, patient's clinic attendances, did not attend rates and admissions in these age ranges.
Results
We had 38 patients with appointments in all three age ranges. The clinic appointments not attended was 2.8% for 15–17-year-olds, 12.9% for 17-19-year-olds and 25.8% for 19-21-year-olds, with significantly more missed in both older age groups compared to the 15-17-year-old group ($P<0.05$). The mean HbA1c increased with each ascending age range, with a significant rise between 15-17 years and 19-21 years (75.7 Vs 80.7, $P<0.05$). Admission rates increased from ten admissions in the 15-17-year-olds to sixteen in the 19-21-year-olds, although the total number of patients contributing to these values increased from six to twelve patients and a higher proportion was due to DKA in the 19-21-year-olds (15-17 years 30% Vs 19-21 years 62.5%).
Conclusion
We have seen an increase in patients not attending clinics through our transition service. Our data demonstrates that our young people are vulnerable heading into adult services, with significantly higher HbA1c values and increasing admission rates, which could have potentially life-threatening consequence. Although we have an integrated transition service, we are not addressing all outcomes (NICE, 2016) with a lack of psychological support after 16 years old and the need to provide social support for our patients and families which a youth worker could address.

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P21

Using language to empower joint diabetes decision making in the paediatric diabetes clinic

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Introduction
Historically there are many examples of doctors using language which does not aid joint decision making with patients. At medical school we are taught to find out the presenting complaint rather than the reason for attendance. We write about non-compliance with treatment in the medical records rather than barriers to adherence. Similarly we use language in the Diabetes clinic which can disempower the children and families who attend our clinics.
Aim
We address how the terminology used in reviewing and describing blood glucose measurements affects children's and young people's perception of the clinic visit and therefore how they would self manage their diabetes after the clinic.
Method
1. Multi-disciplinary staff training to avoid using terms such as good/high and bad/low glucose measurements. The preferred language of the clinic is above or below target range. 2. Questionnaire completed by children and young people attending clinic as well as Paediatric diabetes team to evaluate how different language terms affect diabetes management
Results
Both children and young people together with staff in the diabetes clinic agreed that the use of good and bad as descriptors of blood glucose measurements adversely affected perception of clinic outcome.
Discussion
Increased awareness among MDT diabetes staff on using non-judgemental language when discussing diabetes management with children and families can help improve diabetes control.

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P22

Paediatric diabetes practice overview at a DGH hospital of east midlands deanery

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Introduction and background
Diabetes Mellites is a complex metabolic disorder characterized by chronic hyperglycaemia. Celiac disease & T1DM are immune-mediated diseases that share common susceptibility factors notably HLA genetics. AITD and T1DM are two common autoimmune diseases that can occur concomitantly. It has been proposed that a complex genetic basis together with multiple nongenetic factors make a variable contribution to the pathogenesis of T1DM and AITD. NICE recommends T1DM patients are offered a test for coeliac disease & thyroid disease as they have a higher risk of the Coeliac disease and thyroid disease as compared to the general population. ACDC & KGH NHS Hospital's guidelines recommend checking diabetes auto-antibodies.
Aims
The aim of this audit is to review the local practises and compare them with the guidelines as set out by NICE & ACDC.
Methodology
Data collected for the period of 1st of April 2021 till June 2022. 30 patients studied in this cohort. Ethical approval granted. Data collected using twinkle, Careflow connect and mediviewer
Findings
17 F:13M Initial Coeliac Disease screen done in 97% participants In 2 patients CD screen positive, 1 insufficient sample. 97% of the patients had TFTs done at the time of T1DM diagnosis. None of the cohort tested for TFTs had abnormal TFTs. 94% of patients had T1DM Auto-antibodies checked. 87% of the patients diagnosed with T1DM came back as auto-antibodies positive, while in 2 patients auto antibodies are negative, while 2 had insufficient sample.
Conclusions
97% compliance noted in terms of checking for Coeliac disease, 6% of cohort's CD screen came back as positive. 97% compliance noted for checking TFTs. 94% of patients had T1DM Auto-antibodies checked 87% of the patients were auto-antibodies positive. Checking T1DM auto-antibodies should be part of NICE recommendations to help clinicians understand the T1DM and optimise patient care.
Reference
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Gonadal, DSD and Reproduction

P23

The prevalence of hypertension in children and adolescents with turner syndrome: a systematic review and meta-analysis

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Background
Cardiovascular related deaths account for over 40% of the excess mortality in Turner Syndrome (TS). Hypertension, a modifiable risk factor for both aortic dilatation and dissection, is more commonly encountered in TS during childhood and adolescence. The objective of this systematic review and meta-analysis is to determine the prevalence of hypertension in paediatric patients with TS and in relation to the methodologies of blood pressure evaluation.
Methods
The systematic review of the literature was performed per PRISMA guidelines. Three online databases were searched (Medline, Embase and Web of Science) for literature which reported a prevalence, or allowed calculation of prevalence, of hypertension in patients with TS who were 18 years of age or younger. The primary outcome of this review was the pooled prevalence of hypertension in patients with TS, 18 years or younger. Meta-analysis was conducted using a random-effects model. The between-study variance heterogeneity of effect size estimates across the studies was assessed using the Q-test and the I^2 statistic.
Results
Seventeen studies met the primary eligibility criteria with a total of 1948 patients included. The estimated pooled prevalence of hypertension in children and adolescents TS was 16% (95% CI: 8.9%-24.6%). There was significant heterogeneity detected between the studies. Funnel plot demonstrated no asymmetry and P-value for Egger's test was not significant ($P=0.3123$), suggesting no obvious publication bias. The prevalence of hypertension in studies which utilised 24-hour ambulatory blood pressure monitoring was 21.1% (15.2-27.6). On the other hand, the prevalence of hypertension where blood pressure was obtained from a single measurement was 13.5% (5.2%-24.4%).

Conclusion
To our knowledge, this is the first systematic review and meta-analysis evaluating the prevalence of hypertension in a paediatric TS population. Given the impact of hypertension with long term health outcomes and the reversibility of the health risks by addressing abnormal blood pressure, prompt and early diagnosis of hypertension in young girls with TS should be prioritised. The role of 24-hour blood pressure monitoring in routine clinical assessment of girls with TS should be clarified in future clinical consensus guidance.

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P24

A tale of 2 syndromes

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Background
McCune Albright Syndrome (MAS) is a rare sporadic disorder, affecting 1 in 100,000 to 1 in 1,000,000 people worldwide, with female predilection. It is characterised by a classic triad of fibrous dysplasia (FD) + Café au lait spots (CALs) and precocious puberty. However, in non-classic cases, diagnosis can be made based on 2 or more characteristic features of CALs, FD and Endocrinopathy Mazabraud Syndrome (MS) on the other hand, is a combination of FD + Myxoma. In MS, FD often appear in childhood, the myxoma component appear in adulthood. Both syndromes occur as a result of mutation of the GNAS1 gene which produces G-proteins that help stimulate the activity of an enzyme called adenylate cyclase. GNAS gene mutations result in the constitutive activation of the adenylate cyclase enzyme in many organs vis a vis

- Skin: Café au lait spots
- Ovary: Precocious puberty
- Bone: Fibrous Dysplasia
- Endocrine organs causing autonomous hyperfunction (Thyroid: Hyperthyroidism, Pituitary: Growth Hormone, neonatal Cushing syndrome, phosphate wating excess)

MAS and MS in the same patient is a very rare event, with few reports in the literature.
Method
Here we report a case of childhood onset of MAS and MS.
Case Report
Our patient presented with vaginal bleeding and thelarche at 2 years and was subsequently diagnosed with precious puberty and hyperthyroidism based on hormonal assay. Plain radiography showed multiple patchy areas of bony lysis (ground glass appearance) of the right femur and further workup, with skeletal survey showed a suspicious lesion in the right femur. Follow-up MRI confirmed fibrous dysplasia of the right femur + myxoma Our patient was subsequently diagnosed with Mazabraud syndrome coexisting with McCune-Albright syndrome. She had Aromatase inhibitors with GnRH analogues (as adjuncts to aromatase inhibitors) with good effects. Now at 5 years, she is currently stable and has regular monitoring of bony lesions.
Conclusion
To the best of our knowledge, this is the first case report of childhood onset of MAS and MS. MS associated with MAS has a higher risk of malignant transformation of FD which makes prompt diagnosis and monitoring important.

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P25

Salivary cortisol is increased in paediatric patients with turner syndrome, and the circadian rhythm is blunted: preliminary data from a pilot study

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Background
Increased hair cortisol concentrations are reported in Turner Syndrome (TS) patients compared to healthy controls (HC).(1) Increased cortisol exposure could contribute to cardiovascular, metabolic and bone morbidity in TS. Hair cortisol concentrations give no information about the circadian profile of cortisol, which is important for cardiovascular health. Cortisol is inactivated to cortisone by 11β hydroxysteroid dehydrogenase (11βHSD) type-2 and regenerated from cortisone by 11βHSD type-1. In this pilot study, we compare the circadian profile of salivary cortisol (SC) and cortisone (SCn), and ratio of the same, in girls with TS compared to HCs.(2)
Methods
Saliva samples were collected 30 minutes after waking, every two waking hours for 24-hours and analysed for SC and SCn in girls with genetically confirmed TS. Participants were matched (1:1) for sex-and-age with HCs from the same region.(2)
Results
Ten patients, aged 14.1 ± 2.3years, body mass index (BMI) standard deviation score (SDS) 0.9 ± 1.5 were matched with ten HCs aged 14.1 ± 2.4years, BMI SDS 1.5 ± 1.1. Area under the curve (AUC) for SC was higher in TS girls compared to HC [45.8 (95%CI 17.3-74.2)nmol/l vs 38.4 (95%CI 16.7-60.0)nmol/l] $P = 0.002$. AUC for SCn did not differ ($P = 0.31$). Compared to HCs, the circadian SC profile in TS patients was blunted: morning peak SC was less pronounced, concentrations were higher throughout the morning and declined to concentrations similar to HCs in afternoon samples. In both cohorts the ratio of SCn/SC, increased throughout the day, however this ratio was lower at all time-points, excluding the waking sample, in TS patients.
Discussion
These pilot data support a previous report of increased cortisol exposure in patients with TS, despite higher BMI in HC, which is associated with an increase in SC.(2) The circadian rhythm is intact, but blunted. Differences in the relative activity of 11βHSD 1and2 may contribute to increased cortisol exposure. These findings, and their clinical significance, warrant further investigation in larger cohorts.
We would like to thank the TSSS-UK for their support.
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P26

Gonadotrophin independent puberty (GIPP) with unusually high oestradiol level in an infant with mccune albright syndrome (MAS)

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Background
McCune Albright Syndrome (MAS) is a rare mosaic disease caused by activating mutation in GNAS, characterized by bone fibrous dysplasia, café au- lait (CAL) and hyper functional endocrinopathies (1). GIPP is the most common endocrinologic manifestation seen more frequently in girls (2). In a few studies, letrozole, tamoxifen, or fulvestrant were effective in decreasing the rate of skeletal maturation and vaginal bleeding (3,4,5).
Case Report
A 3-month-old female infant presented with vaginal bleeding for 5 days. On examination she had CAL and firm prominent breast. Investigations were consistent with GIPP. Oestradiol levels was 1552 pmol/l (<44 pmol/l) with undetectable gonadotrophins. Ultrasound showed bilateral ovarian cyst maximum diameter 7 mm. On our initial evaluation, bleeding had self-resolved and oestradiol levels were 828 pmol/l. We decided to wait and watch. At 7 months there was again breast enlargement, Oestradiol levels peaked at 8364 pmol/l. Scans showed reoccurrence of ovarian cysts, the left side larger than the right (56 mm x 49 mm x 35 mm). The uterus was enlarged for age. Tumour markers (AFP/BHCG) were negative. Skeletal survey revealed significantly advanced bone age of I year 9 months at a chronological age of 0.66 years (Z score 5.37). After MDT discussions we commenced Cyproterone acetate 10 mg BD (50 mg/m^2/day) rather than Anastrozole as there was increased risk of torsion with the latter. We also involved the surgical team and agreed surveillance scans 2 weekly. Given the cyclical nature of cysts, surgical intervention would only provide short-term solution with high chance of ovarian damage. Over the coming months we continued surveillance with regular scans. Follow up oestradiol levels rose (~3000 pmol/l) with increase in ovarian cyst size. This waxing and waning pattern of the ovarian cyst despite being on Cyproterone acetate warranted further treatment. Tamoxifen was added to block the effect of oestradiol on the uterus and bone age. She has radiological evidence of fibrous dysplasia involving the orbit but no evidence of compression on optic nerve.
Conclusion
This case highlights complexity involved in management of ovarian cysts in infancy.

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P27

Delayed puberty is very common in boys with duchenne muscular dystrophy on daily glucocorticoid-implications for management and age to initiate testosterone

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Objectives
Delayed puberty is thought to be common in boys with Duchenne muscular dystrophy [DMD]. To date, studies addressing its frequency are not available. This study aims to report the frequency of delayed puberty in DMD from clinical examination.
Methods
All boys with DMD aged at least 14 years in January 2022 known to the Glasgow paediatric neuromuscular service (2015-2022) were included. Thirty-seven boys were identified. All 37 boys had at least two clinical assessment of puberty by a paediatric endocrinologist between 12 to 18 years. Delayed puberty was defined based on testes volume and/or genital staging in comparison to puberty normogram [van Buuren *et al* 2013].
Results
Median latest age was 17.1 years (Range 14.0-22.9). Of the 37 boys, 25 (68%) had delayed puberty. Twenty-three boys were treated with testosterone for at least six months. Of the 25 with delayed puberty, 88% were on daily glucocorticoid between 12-14 years but only 50% of those with normal onset of puberty were on daily glucocorticoid ($P<0.05$). Only one boy (4%) with delayed puberty was not treated with glucocorticoid between 12-14 years; but 42% with normal onset of puberty were not treated with glucocorticoid. Delayed puberty was present in 79% of boys on daily glucocorticoid. In those with delayed puberty, 76% had a history of fragility fractures; but of those with normal onset of puberty, only 33% had fragility fractures ($P<0.05$). Two of 10 (20%) with delayed puberty who were treated with testosterone in adolescence remained hypogonadal as young adults. Early morning testosterone levels were <8nmol/l on two occasions and both recommenced adult replacement therapy.
Conclusion
Almost 80% of adolescents with DMD on daily glucocorticoid had evidence of delayed puberty. Our data calls for the consideration of testosterone therapy from an earlier age in boys on daily glucocorticoid than the generally accepted age of 14 years. Preliminary results suggest that a small percentage of men with DMD and delayed puberty remained hypogonadal as young adults despite achieving adequate adult secondary sexual characteristics with testosterone. Clarifying gonadal function at the time of transition is important, and clinical pathways should be developed.

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P28

Extreme overgrowth resulting from exposure to exogenous testosterone gel in a young boy

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Background
Pseudo precocious puberty in young children usually arises from adrenal or less commonly testicular causes. Though rare, the possibility of an exogenous source should also be considered.
Case Report
A 2 year 2 month old male child presented with apparent overgrowth since about 1 year of age. His height was 108 cms [+6.29 SDs], weight 21 kgs [+4.54 SDs] and head circumference 52.2 cms [2.76 SDs]. He looked very mature for his age but had no dysmorphic features. He had significant penile development and stage 2 pubic hair but small testes. He also had morning erections and challenging behaviour but was developmentally age appropriate. Investigations confirmed a raised testosterone 3.4 nmol/l and IGF1 35.1 nmol/l but normal thyroid function and random cortisol. A urinary steroid profile excluded congenital adrenal hyperplasia and adrenal tumours and an abdominal ultrasound was normal. Shortly afterwards, the testosterone was repeated and was now 14.1 nmol/l; a GnRH test was unsuccessful but the basal gonadotrophins were undetectable. The plasma adrenal androgens were also low. His bone age was very advanced at 4.6 years. On further enquiry, it emerged that his father, who was an active carer, has been using daily topical testosterone gel for hypogonadism for over 2 years. His metered dose totalled 60.75 mg daily and was applied every morning to his bare hands and then transferred to his shoulder areas. He said he washed his hands after application. He was asked to stop using the gel and consider alternative replacement treatment: a repeat testosterone level in the child one month later was undetectable.
Discussion
Transfer of topical testosterone gel between adults, often between sexual partners, is well known but is rarely recognised in children. Apart for the exclusion of other causes of a raised testosterone in a young child, the extreme variation in the measured testosterone level was highly suggestive of an exogenous source. Routine enquiry about family use of testosterone gels should considered in pseudo precocious puberty in young children.

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Miscellaneous 1

P29

Trametinib induced hyponatraemia in a patient with craniopharyngioma and diabetes insipidus

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Background
Adamantinomatous craniopharyngiomas (ACPs) are rare, benign, epithelial tumours of the sellar-suprasellar region. Craniopharyngiomas cause considerable morbidity and mortality due to local invasion and treatment-related damage to surrounding structures, including the hypothalamus and pituitary gland, leading to hypopituitarism and diabetes insipidus (DI). Trametinib is a highly selective mitogen-activated protein kinase (MEK) inhibitor, which has been recently used in the management of treatment-resistant brain tumours, including suprasellar low-grade gliomas, papillary craniopharyngiomas and Langerhans cell histiocytosis, by inhibiting the oncogenic MEK/ERK pathway. Despite being thought to have less side effects, off-target toxicities of such molecular therapies such as hyponatraemia have been described.
Case report
An 11-year-old girl presented with multiple relapses of an ACP which was initially diagnosed at age 3-years. Due to multiple progressions, she underwent several decompressive surgeries, proton beam therapy and Ommaya reservoir insertion. She developed a left hemispheric stroke post-irradiation and a right hemispheric stroke following surgical resection. Panhypopituitarism and optic atrophy were already present at diagnosis, and she subsequently developed hypothalamic obesity and impaired glucose tolerance. She had multiple episodes of adrenal crises and her DI was difficult to manage, required gradual escalation in desmopressin doses up to 1.4 mg/day in 5 divided doses. Multiple solid and cystic progressions led to increasing lethargy, headaches and decreased quality of life, requiring cyst aspiration every 7-10 days, providing temporary but not sustained improvement. A trial of Trametinib was commenced given positive immunohistochemistry for phosphor-ERK. At commencement, she had a serum sodium of 132 mmol/l. After one week, she presented with abdominal pain, diarrhoea, drowsiness and collapse with hyponatraemia (120 mmol/l) whereby desmopressin was withheld. Her desmopressin was restarted gradually and she was stabilised on 150 micrograms/day (11% of her original dose) to maintain eunatraemia.
Conclusion
Hyponatraemia is a known side-effect of Trametinib, hypothesised to be due to insertion of aquaporins into the renal tubules, and increased renal free water reabsorption. As such, patients with known DI need close sodium monitoring and close review of desmopressin doses when starting Trametinib under the supervision of a paediatric endocrinologist.

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P30

Risk of post-treatment hypothyroidism in paediatric neuroblastoma

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Background
Neuroblastoma investigations and treatments are associated with thyroid dysfunction. This study aims to identify the consequences of different neuroblastoma investigations and treatments on the thyroid status of patients.

Methods
This is a retrospective cohort study of neuroblastoma patients at a tertiary paediatric endocrinology/oncology centre. Electronic records were reviewed for previous treatments (chemotherapy, surgery, radiotherapy, anti-GD2, IL-2), number of MIBG scans and thyroid function tests post-treatment. Out of 212 patients identified, 41 had a complete set of data. The data was analysed to understand the correlation between treatment modalities, MIBG scans, and the consequent development of hypothyroidism.
Results
12/41 (27.9%) patients developed primary hypothyroidism. Treatment modalities included chemotherapy and surgery ($n=1$, 8.3%), chemotherapy ($n=1$, 8.3%), chemotherapy, surgery and radiotherapy ($n=3$, 25%), chemotherapy, radiotherapy, surgery, anti-GD2 and IL-2 ($n=3$, 25%) and chemotherapy, surgery, radiotherapy and anti-GD2 ($n=4$, 33.3%). 5/26 (19.2%) and 7/15 (46.7%) patients receiving <5 and ≥ 5 MIBG scans respectively developed hypothyroidism ($P=0.06$). 3/6 (50%) patients receiving IL-2 and 9/35 (25.7%) not receiving IL-2 developed hypothyroidism ($P=0.2$). 7/16(43.8%) patients on anti-GD2 and 5/25 (20%) patients not receiving anti-GD2 developed hypothyroidism ($P=0.07$). 5/10 (50.0%) patients received both anti-GD2 and ≥ 5 MIBG scans developed hypothyroidism compared to 2/6(33.3%) of those receiving anti-GD2 treatment but <5 MIBG scans and 2/5 (40.0%) receiving ≥ 5 MIBG scans but not anti-GD2 treatment. ($P=0.80$). The only patient receiving both IL-2 and ≥ 5 MIBG scans also developed hypothyroidism compared to 2/5 (40.0%) patients receiving IL-2 but <5 MIBG scans and 6/14 (42.9%) receiving ≥ 5 MIBG scans but not IL-2 treatment.
Conclusion
There was a non-statistically significant trend towards an increased frequency of post-treatment hypothyroidism in patients receiving ≥ 5 MIBG scans and anti-GD2 treatment in this paediatric cohort. The combination of anti-GD2 and IL-2 with higher numbers of MIBG scans did not result in a higher risk of hypothyroidism.
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P31

Clinical features of multiple endocrine neoplasia type 1 in children
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Background
Multiple endocrine neoplasia type 1 (MEN1) is a rare autosomal dominantly inherited condition predisposing to primary hyperparathyroidism (PHPT), pituitary tumors, gastroenteropancreatic tract neuroendocrine tumors (NET), thymic tumours and skin lesions. Clinical features are rare in the paediatric population and guidance exists on the screening for complications of MEN1.
Objective
To describe clinical features and treatment outcomes in a single cohort of MEN1 patients under a tertiary paediatric endocrine centre.
Methods
Demographic and clinical data from patients with confirmed MEN1 mutations who commenced tumour surveillance aged ≤ 18 years under the Evelina London Children's Hospital in 2015-2022 were collected and analysed retrospectively. Results are presented as median (ranges).
Results
This cohort included 14 patients (7 Males), aged 12.7 (6.3-17.8) years who had undergone predictive genetic testing (5 paternally, 9 maternally inherited MEN1 mutations) at aged 8.6 (6.4-13.2) years. Tumour surveillance started 0.65 (0-3.3) years post diagnosis. MEN1-related manifestations occurred in 9 (6 Males) patients, with the first abnormality detected aged 13.7 (6.6-16.5) years, among which 6 presented asymptomatically after 4.15 (1.6-5.5) years of screening. PHPT presented in 4 (28%) patients aged 12.0 (6.6-13) years. One patient (aged 17 years) had subtotal parathyroidectomy for persistent hypercalcaemia from parathyroid hyperplasia. Imaging identified pituitary microadenomas (PTA) in 4 (28%) patients aged 14.4 (11.9-15) years including 2 nonfunctioning and 2 microprolactinoma, of which, 1 was treated with dopamine-agonist. Pancreatic tumors were diagnosed in 5 patients aged 12 (10.6-14.7) years including 1 insulinoma, 2 pNET, 2 non-functioning adenomas (<2 cm). The insulinoma patient presented with neuroglycopenic symptoms aged 10.6 years and underwent a partial pancreatectomy at 10.8 years. Two patients had pancreatic NET (pNET) confirmed on tissue biopsies (aged 15.8 and 16.4 years) and were both treated with somatostatin analogues. Concurrent manifestations occurred aged ≤ 18 years in 3 (21%) patients: PHPT and PTA ($n=2$); PHPT, PTA and pNET ($n=1$).
Conclusions
MEN1-related pathology in the paediatric population results in significant morbidity. Our findings highlight the importance of initiating screening early in childhood, recognizing the need to achieve balance between the practicalities, costs and consequences of screening vs the usefulness in identifying and managing pathology.
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P32

Service evaluation of girls with complex disability presenting with concerns regarding puberty
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Introduction
There are currently no recommendations on the assessment, investigation and follow-up for girls presenting with concerns regarding puberty with background of complex disability who are non-weight bearing.
Aim
Service evaluation (assessment, investigation and follow-up) of girls presenting with any of Central Precocious Puberty (CPP), Early Puberty (EP), Delayed Puberty (DP) or period management with background of immobility in context of complex disability.
Methods
Girls identified from two New Paediatric Endocrine clinics, 2016-2019. Information including age, pubertal status, diagnoses, medication, nutrition and fracture history was collected.
Minimal standards of care were established:
- Height/length, weight and pubertal assessment
- Biochemical assessment of puberty (Follicle Stimulating Hormone [FSH], Luteinising Hormone [LH] and oestradiol)
- Bone age and pelvic ultrasound (CPP/EP/DP only)
- Assessment of bone health (Dual X-ray Absorptiometry [DXA] +/- lateral spine x-ray, vitamin D and bone profile)

Results
13 girls were included with background of immobility secondary to cerebral palsy ($n=6$), spina bifida ($n=5$) or other developmental delay ($n=2$). Median age was 9.5years (range: 0.9-15.0). Assessment of height/length was recorded in 6/13(46.2%), weight in 9/13(69.2%) and pubertal assessment in 10/13(76.9%) girls. FSH, LH and oestradiol were measured in 10/13(76.9%) girls. Bone age was performed in 7/7(100%) and pelvic ultrasound in 5/7(71.4%) girls presenting with CPP/EP/DP. 5/13(38.5%) girls had an assessment of bone health with either DXA ($n=2$) or spinal x-ray ($n=3$). Vitamin D and bone profile was measured in 7/11(53.8%) girls. All 13 girls were followed up at least once with final diagnoses CPP ($n=2$), EP ($n=4$), DP ($n=1$) and period management ($n=4$). Treatment was commenced in 10/13(76.9%): 7/10(70%) received Gonadotropin Releasing Hormone analogue, 2/10(20%) supplemental oestrogen, 1/10(10%) Tranexamic acid and Mefenamic acid.
Conclusions
A leaflet titled "Managing Puberty in Young Girls with Physical and Learning Disabilities' was produced to provide information to parents and carers. A proforma was created to guide assessment of puberty and bone health in complex disability.
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P33

Cardiac imaging in a dedicated paediatric turner syndrome clinic
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Background
Turner Syndrome (TS) is a complete or partial loss of the second X chromosome affecting approximately 1:2000 females, classically associated with short stature

and hypogonadism. Cardiovascular complications in TS include increased risk of congenital cardiac malformations, hypertension, ischaemic heart disease and aortic dissection. Cardiovascular related deaths account for over 40% of the excess mortality in TS and requires lifelong monitoring and follow-up. The Clinical Practical Guidelines for the Care of Girls and Women with Turner Syndrome (published 2016) have provided recommendations for clinicians regarding frequency of cardiac imaging.
Methods
Girls attending a dedicated paediatric TS clinic at the Royal Hospital for Children Glasgow, from 2015-2020, were included. Information collected included age, age of diagnosis of TS, identified cardiac abnormality, hypertension, imaging type and frequency. The frequency of imaging (including echocardiogram and MRI) was obtained from a departmental database and compared to published recommendations.
Results
51 girls with a median age of diagnosis of 0.83 years (range 0-16.71) were included. 32/51 (63%) girls had an echocardiogram performed within 6 months of diagnosis. 22 girls transferred to adult care during the 5-year study period. 14/12 (64%) girls had an echocardiogram performed in the two years prior to transfer to adult services. 21/51 girls met criteria to have biennial cardiac imaging: 28% attained this prior to 2016 and 40% after 2016 (NS). 30/51 girls met the criteria to have cardiac imaging every 5 years: 43% attained this prior to 2016 and 52% after 2016 (NS). Echocardiography was the most common imaging modality used.
Conclusions
Currently in our centre not all girls are routinely referred for cardiac imaging at the recommended time intervals. Further evidence supporting the implementation of regular routine imaging is required for this to be deemed practical in most paediatric centres.

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P34

Digitising patient information leaflets using QR codes

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Background
Patient information leaflets are widely used by clinicians to reinforce and supplement information discussed during a consultation. This helps empower the patient and their family by enabling them to gain a greater understanding about their condition, investigation and/or treatment. However, despite the global increase in digital activity leaflets are still being disseminated in printed form. Accessing them online may be the more preferable option and would also more environmentally friendly, reducing the large number of leaflets that need to be printed on a daily basis.
Aim
Compile regularly used information leaflets in the Paediatric Endocrinology department of Evelina London Children's Hospital and develop a method for them to be accessed online. The aim is to save the clinician time spent searching for leaflets and enable easier dissemination.
Methods
Information leaflets were collated from the websites of the European Society of Paediatric Endocrinology (ESPE), British Society for Paediatric Endocrinology & Diabetes (BSPED), Scottish Paediatric Endocrine Group (SPEG) as well as resources created by clinicians from Evelina London. The URLs to these leaflets were converted into QR codes using an online website (qrcodechimp) and organised into categories such as Adrenal, Growth, Pituitary etc. on a single document. Additional subcategories were highlighted such as Tests (Oral Glucose Tolerance Test, Arginine Test) and also Easy Readability leaflets – These are targeted towards young children facilitating their involvement and improving understanding about their disease.
Results
Clinicians have access to a single document consisting of QR codes for all the regularly used information leaflets. The categories ensure the required leaflet is found quickly so more time can be dedicated towards the patient. Patients and families can use their mobile phones to scan the QR code for the appropriate leaflet.
Conclusion
Online information leaflets need to be made more accessible especially considering the current digital age and environmental impact of the medical industry. Further research could be done comparing the effectiveness of physical and digital leaflets for both the patient and clinicians.

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P35

A Perfect storm: multisystem endocrine disorders in a girl with T21

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Introduction
Down Syndrome is the commonest genetic disorder with a frequency of 1 in 700 births. Amongst many features associated with this condition, autoimmune and non-autoimmune endocrine disorders are some of the commonest manifestations. We present the case of a child with Down Syndrome with multiple autoimmune endocrine disorders and discuss the challenges she will face in her management as well as upon transition to adult services.
Case Report
A 15 year 11 month old girl was admitted due to a 2 month history of vague right flank pain, intermittent vomiting, fatigue and reduced appetite and new periocular hyperpigmentation. A significant background of autoimmune hypothyroidism and T1DM since the age of 5 and 10 years old respectively, as well as secondary amenorrhoea since menarche at age 14 and elevated gonadotrophins were noted. During admission she was hypotensive and she required IV fluids due to extremely poor oral intake. Whereas she previously had good blood glucose control she was now experiencing frequent hypoglycaemic episodes. Laboratory workup revealed borderline hyponatraemia with normal serum potassium levels. Early morning cortisol was low and Short Synachten Test failed to demonstrate a serum cortisol rise in response to synthetic ACTH. Serum renin was raised, aldosterone was low, 17 – OHP levels were normal. Anti-adrenal gland antibodies were detected. Our patient was diagnosed with autoimmune primary adrenal insufficiency. She commenced hydrocortisone and fludrocortisone replacement with doses uptitrated as per clinical and biochemical response. Her hypoglycaemic plan was updated to include IM Hydrocortisone administration prior to IM Glucagon in case of severe hypoglycaemia. Pelvic ultrasound demonstrates a small uterus and difficulty visualising the ovaries. Anti – ovarian antibodies are present thus indicating autoimmune ovarian insufficiency.
Conclusion
Our case demonstrates the complexity of autoimmune endocrine disease in the context of Down Syndrome. Careful consideration to management of hydrocortisone replacement, diabetic control and thyroid function surveillance will be needed on an ongoing basis. Unfortunately, literature shows that transition to adult services for children with Down Syndrome is not as successful as other children with chronic medical conditions therefore highlighting a required area of improvement going forward.

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Obesity 1

P36

Percentage excess weight and risk of co-morbidity in obese children

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Background
One in four children in England are now obese by school year 6. Childhood obesity is associated with significant co-morbidity including type 2 diabetes (T2DM), non-alcoholic fatty liver disease (NAFLD), obstructive sleep apnoea (OSA) and depression. NICE guidance suggests consideration of co-morbidity screening in children with body mass index (BMI) >98th centile but BMI does not accurately reflect adiposity in children owing to confounding effects of gender, height, ethnicity and puberty. We hypothesised that percentage excess weight (%EW) better predicts co-morbidity than BMI standard deviation score (SDS).
Method
We reviewed data from the last 100 patients seen in our tertiary paediatric weight management clinic. Ideal weight was determined by the weight on the same centile as the height centile. %EW was calculated by: actual weight minus ideal weight, divided by the ideal weight and multiplied by 100 (all in kilograms). Statistical analysis was performed using SPSS version 26.
Results
Patients were aged range 2-18 years, (65% were male). %EW was 11-181 (median 79). BMISDS was 1.84-7.75 (median 3.82). Weight-related co-morbidity was detected in 85% (85/100) patients: 55% (40/73) had insulin resistance (Homeostatic Model Assessment for Insulin Resistance (HOMA-R) >4), 6.3% (2/32) had T2DM on oral glucose tolerance test, 39.7% (31/78) had dyslipideamia, 42.6% (40/94) had NAFLD (raised alanine aminotransferase +/- ultrasound), 45% (14/31) had OSA, 25.6% (11/43) were hypertensive (systolic BP>90th centile) and 25% (25/100) had formal treatment for anxiety or

depression. Forty percent of all patients had a co-morbidity diagnosed prior to referral (30.7% (8/26) of patients with >100%EW). %EW positively correlated to the number of co-morbidities (rs = 0.23, $P = 0.02$) and to HOMA-R (rs = 0.34, $P = 0.004$). BMISDS did not correlate with co-morbidities or HOMA-R (p 0.73 and 0.79 respectively). A co-morbidity was present in all children with ≥100%EW weight and 85% of those with >50%EW.
Conclusion
Unlike BMISDS, %EW correlates to the number of weight-related co-morbidities and HOMA-R. All patients with ≥100%EW had at least one weight-related co-morbidity, with no comparable BMISDS cut off. Co-morbidity was likely underrepresented due to high was-not-brought rates and limited availability of testing. We suggest %EW is a useful, accessible and understandable predictor of weight-related co-morbidity.

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P37

Obesity in glucocorticoid treated boys with duchenne muscular dystrophy: a need for structured nutritional-metabolic assessment and pro-active management

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Background
Glucocorticoid (GC) therapy is standard of care of management of Duchenne Muscular Dystrophy (DMD) but its use is associated with a range of side-effects. Weight gain leading to significant obesity is common in GC-treated boys.
Aim(s)
To evaluate changes in growth parameters: height-SDS, weight-SDS, body mass index (BMI)-SDS following initiation of GC in DMD.
Methods
Between 2013-2019, 26 boys with DMD were commenced on daily GC. Growth parameters at baseline, 1-year and 2-years were compared. Data were expressed as mean (SD). $P < 0.05$ was accepted as statistical significance.
Results
Of the 26 boys, 1 was excluded due to insufficient growth data at follow-up. All 25 boys were initiated on daily GC (15 Deflazacort, 10 Prednisolone), and remained on the same GC regimen/type during the 2-year follow-up. Mean age at initiation of GC was 5.5 years. All boys remained ambulant all throughout the 2-year follow-up. Mean height-SDS prior to initiation of GC at baseline was -1.15 (1.12). Mean height-SDS at 1-year was -1.57 (1.10) [$P < 0.001$ vs baseline] and was -1.87 (1.01) at 2-year [$P < 0.001$ vs baseline and 1-year]. Mean BMI-SDS at baseline was +0.67 (0.97). Mean BMI-SDS at 1-year was +1.08 (1.1) [$P = 0.009$ vs baseline] and was +1.46 (0.96) at 2-year [$P < 0.001$ vs baseline; $P = 0.002$ vs 1-year]. At baseline, BMI-SDS in the overweight, obese or severely obese category was noted in 5/25 (20%) whereas this was noted in 9/25 (36%) boys at 1-year and 13/25 (52%) at 2-years of GC treatment. The proportion of boys with severe obesity at baseline was 1/25 (4%) and 3/25 (12%) at 1-year and 2-years, respectively. Investigations for metabolic complications were not performed in overweight, obese or severely obese boys.
Conclusion
Significant increase in BMI occurs early following initiation of daily GC in young boys with DMD. Routine structured nutritional input should be part of clinical care at the time of initiation of GC. Current management strategies of childhood obesity and its complications are not suitable for boys with DMD (e.g. exercise and use of statins contraindicated). National clinical pathways of evaluation and management of obesity-metabolic complications in DMD should now be developed.

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P38

A questionnaire-based baseline evaluation of hunger in UK adolescents with severe obesity

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Introduction
Evaluating hunger and hyperphagia is an important component of assessing children and young people with obesity. Identifying increased hunger levels will help clinicians and health professionals to taper management aspects including relevant genetic testing and providing tailored dietary and pharmacological management.
Aim
The aim of this study was to evaluate the baseline hunger levels in a group of UK adolescents with severe obesity.
Methods
Individuals who attended a paediatric tier 3 weight management clinic completed the three-factor eating questionnaire-R18 (TFEQr18) at baseline. This validated measure focuses on cognitive restraint, uncontrolled eating, and emotional eating.
Results
39 patients completed the questionnaire, with an average age of 14.7 years (range 12-17). 51.3% (20/39) were female. The median body mass index (BMI) was 43.5 kg/m^2 (IQR 39.8-48.6). The transformed scores for each category were scored out of 100. The median score for uncontrolled eating was 44.4/100 (IQR 25.9-62.9) and for cognitive restraint was 40/100 (IQR 30.6-51.7). Emotional eating was the highest of the three categories with a median score of 55.6/100 (IQR 22.2-72.3). These results are higher than those published for individuals with a BMI within the normal range. When analysed using linear regression, with BMI as the independent variable, there was no association found between BMI and the three categories probably because all the BMI measurements are over 30 kg/m^2.
Discussion
The results of the baseline TFEQr18 questionnaires completed by adolescents with significant obesity have shown higher scores in the emotional eating and uncontrolled eating categories, with cognitive restraint scoring lowest. This information would be useful for the multidisciplinary team to provide targeted therapy and to monitor the response to the management.

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P39

Baseline body composition of adolescents attending a UK tertiary weight management service

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Introduction
Visceral body fat has been shown to correlate with complications related to obesity. Body mass index (BMI) is widely used to define obesity in the adolescent population; however, it does not take the overall body composition into account. We present body composition data in a group of UK adolescents attending the tertiary MDT weight management service.
Methods
Data was collected on 31 patients (M:F = 15:16) attending the MDT service over a 6-month period. Body composition was evaluated by bioelectrical impedance analysis using TANITA RD-545 body composition scale.
Result
The mean (±SD) age was 14.56 years (range between 12-18 years) and the average weight was 123.12 kg (±25.15). The mean BMI and BMI SDS were 43.15(±7.67) and 3.67(±0.48) respectively. The mean fasting insulin and C-peptide were 338 pmol/l and 1617 pmol/l respectively. The OGTT did not reveal evidence of diabetes or pre-diabetes in the group. 7/31 (23%) patients had abnormal liver function and 39% (11/37) had dyslipidaemia. The mean fat mass (FM) was 57.05 kg (±16.06SD) and fat free mass (FFM) was 63.33 kg (±12.6SD) in males. In females, the mean fat mass (FM) was 68.19 kg (±22.096SD) and fat free mass (FFM) was 56.8 kg (±8.6SD) which were significantly elevated. Body fat percentage was 46.15% in males and 53.64% in females. There was a positive corelation between BMI SDS and body fat percentage in both males [$r = 0.773$, $P = 0.0019$] and females [$r = 0.785$, $P = 0.0015$] which was statistically significant ($P < 0.01$). 19 (61%) patients were managed with lifestyle modification and behavioural intervention. 11(34%) patients were started on GLP1 analogue therapy after a period of lifestyle intervention.
Discussion
Our data provides insights into the baseline body fat composition in a group of adolescents with significant obesity. Assessment of fat mass and fat free mass could help providing targeted interventions in achieving weight loss. Serial assessment of body composition and FFM/FM ratio could help monitor the response to lifestyle intervention and medical therapy for weight management. Improving muscle mass and reducing fat mass will have positive impact on

metabolic parameters and long-term cardiovascular outcomes in adolescents with severe obesity.

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P40

Thrombocytopenia in a patient on antiretroviral therapy treated with liraglutide

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Introduction

Up to 70% of adults living with human immunodeficiency virus (HIV) have excessive weight due to side effects of antiretroviral therapy (ART). Liraglutide is a licenced GLP-1 receptor agonist for the treatment of obesity in adolescents. However, there are no studies on effectiveness and safety of GLP-1 receptor agonists in patients on ART as these patients are excluded from most of the clinical trials. Herein, we present a teenage girl with HIV who developed thrombocytopenia after commencing Liraglutide treatment.

Clinical case

A 15-year-old female on ART for perinatally acquired HIV was referred to the endocrine team with excessive weight gain since the age of 7 years. The patient had been on the dolutegravir containing ART regimen for the previous 2 years with normal CD4 levels and undetectable HIV viral load. She had also suffered with intermittent episodes of non-bloody diarrhoea for >2 years, cause was unknown. Examination revealed normal height of 163.4 cm (SDS 0.13), excessive weight of 131 kg (SDS 7.66) with a very high BMI of 49.1 kg/m^2 (SDS $+4.05$). She had no clinical features that indicated underlying endocrine causes for the obesity. As the lifestyle changes were not successful due to complex social circumstances, the patient was commenced on Liraglutide at the dose of 0.6 mg/day which was gradually increased to 1.8 mg/day. Liraglutide helped to reduce her appetite, but she complained about bruising at the injection sites. Three weeks after commencing Liraglutide, a drop of platelet count was noticed (from $312x10^9$/l to $27x10^9$/l). A week after Liraglutide was stopped, platelet count increased to $41x10^9$/l. Full blood count showed normal level of erythrocytes and moderately increased leucocytes and lymphocytes. Past medical history revealed previous drop of platelet count during Epstein-Barr virus (EBV) infection at the age of 8 years (repeat PCR for EBV is pending).

Conclusion

Liraglutide has successfully decreased appetite in our patient with significant obesity and stable on ART. The patient is keen to recommence treatment. The cause of thrombocytopenia is unclear. Immune thrombocytopenia due to an intercurrent viral infection is plausible. To the best of our knowledge, Liraglutide-related thrombocytopenia has not been previously reported.

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Pituitary and Growth 1

P41

Use of the U.K. 100,000 genomes project to identify the genetic basis of childhood pituitary disorders within a tertiary paediatric endocrinology centre

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Introduction

The UK 100,000 Genomes Project (100KGP) investigated the genetic basis of rare disease. The molecular drivers of most paediatric pituitary disease remains unknown.

Methods

Children with genetically unexplained pituitary disorders attending a tertiary paediatric endocrinology centre were recruited to the 100KGP and underwent whole genome sequencing. Parental DNA was obtained where feasible. Virtual gene panels were applied and bioinformatic pipelines used for variant filtering. A variant was considered a finding if it met ACMG pathogenicity criteria and if it was relevant to the phenotype as assessed by a multidisciplinary endocrine and genetic team.

Results

A total of 140 children were recruited (61.8% male ($n=89$)). Diagnoses included septo-optic dysplasia (39.6%, $n=57$), congenital hypopituitarism (32.6%, $n=47$), isolated growth hormone deficiency (17.9%, $n=25$), growth hormone neurosecretory dysfunction (2.8%, $n=4$), hypogonadotropic hypogonadism (4.9%, $n=7$) and holoprosencephaly (2.8%, $n=4$). Multiple pituitary hormone deficiencies were present in 62.5% ($n=90$). Most children had structurally abnormal pituitary glands (87.5%, $n=126$). A genetic diagnosis was obtained in 20.1% ($n=29$) of children (65.6% trios ($n=19$); 34.5% duos/individuals ($n=10$)). Heterozygote variants were detected in 72.4% ($n=21$) in *N2RF1, ACTB, TGIF1, PTPN11, KRAS, DPF2, SMC3, ZNF148, FGFR1, FGFR3, SIX3, GRIN2A, GLI2, CLCN7, EP300, TBL1XR1*, and *GHRHR;* de novo in 23.8% ($n=5$). Homozygous or compound heterozygote variants were found in 27.6% ($n=8$) within *GLI2, PKHD1, CHD7, DHTKD1, GHRHR*, and *TBC1D32*. One child carried variants in both *GLI2* and *LHX4*. Children with extra-endocrine features were more likely to have a genetic finding identified compared to those with solely endocrine presentations (27.6% vs 8.8%, $P=0.006$). A finding was confirmed in 15.8% of children with septo-optic dysplasia compared to 23.8% of those with other pituitary conditions and in 28.0% of those with development delay compared to 16.0% of those without. There were no significant associations between obtaining a genetic diagnosis and patient gender, pituitary gland structure, or number of pituitary endocrinopathies.

Conclusion

The 100KGP facilitated a novel approach to diagnosing the molecular basis of paediatric pituitary disease. We demonstrate the importance of using a transparent, process-driven, multidisciplinary approach to variant classification and the value of integrating next generation sequencing approaches into standard clinical care.

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The endocrine phenotype of SWI/SNF-associated coffin-siris syndrome includes pituitary endocrinopathies, pituitary hypoplasia, and septo-optic dysplasia

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Introduction

Coffin-Siris Syndrome (CSS) is a rare multisystem genetic disorder which often arises from genetic abnormalities within genes encoding for the SWI/SNF complex (*ARID1A, ARID1B, DPF2, SMARCA4, SMARCB1, SMARCA2, SMARCE1*). Endocrine abnormalities previously associated with this disorder include idiopathic short stature, hyperinsulinism, obesity, growth hormone deficiency, and cryptorchidism. We describe the endocrine features and associated radiological findings of a series of children with SWI/SNF-associated CSS.

Results

A total of eight children with CSS caused by pathogenic variants in the SWI/SNF complex attend our tertiary endocrine centre (*ARID1B* $n=6$; *ARID1A* $n=1$; *DPF2* $n=1$). Of the six children with *ARID1B* variants, one has confirmed growth hormone deficiency (GHD) with pituitary hypoplasia (*ARID1B*, c.1518dupC, p.Gly507fs) and one has short stature, bilateral undescended testes, and a hypoplastic corpus callosum. Two others do not have endocrinopathies but have abnormal pituitaries and/or septo-optic dysplasia (*ARID1B*, c.4063C$>$T, p.Gln1355*; *ARID1B* c.5993_5994del, p.Glu1998Glyfs*3). The fifth child has a normal pituitary gland, polycystic ovarian syndrome, insulin insensitivity, and anosmia (*ARID1B*, c.3862$+$1G$>$A). The sixth has no endocrine nor pituitary abnormalities (*ARID1B*, c.5345del, p.Ser1782Ilefs*8). The child with the *ARID1A* variant (c.1213C$>$T, Gln405*) has septo-optic dysplasia with no endocrinopathies. The child with the *DPF2* variant (c.894_904$+$6del; p.Cys298Trpfs*38) has delayed puberty, GHD, and anterior pituitary hypoplasia.

Discussion

CSS exhibits a complex, multisystem phenotype. We expand the spectrum of SWI/SNF-associated Coffin-Siris syndrome to include pituitary endocrinopathies,

anterior pituitary hypoplasia, and midline brain abnormalities on the septo-optic dysplasia spectrum. This is consistent with the phenotype seen in mice heterozygous for *Arib1b* loss-of-function variants. The SWI/SNF complex modulates chromatin structure and carries key roles in transcription and cell differentiation, which may explain the aberrant pituitary development seen in a subset of patients with CSS.

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P43

Neurobehavioural impairments in children with septo-optic dysplasia: a scoping review

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Background
Septo-optic dysplasia (SOD) is a rare congenital condition diagnosed in children with two or more of hypothalamo-pituitary axis dysfunction, midline brain abnormalities, and optic nerve hypoplasia. SOD has a heterogenous clinical phenotype, characterised by varying visual impairment and endocrine dysfunction. Autistic-like behaviours have also been reported in children with SOD, however the nature of these neurobehavioural impairments remain to be fully understood.
Objectives
The aim of this scoping review was to address the following research questions: What is the prevalence of neurobehavioural impairments in children with SOD? What standardised measures have been used to assess these impairments?
Methods
The search was conducted in PubMed and OVID databases EMBASE and PsychInfo. Hand-searching reference lists of included studies was conducted to search for additional papers. All peer-reviewed, observational studies assessing cognitive, behavioural, emotional, and social impairments, or autism spectrum disorder (ASD) symptoms were retrieved. Due to heterogeneity in the diagnostic classification of SOD, children (<18 years) with SOD, ONH, and SOD-plus were included. Studies were excluded if they did not use standardised measures of neurobehavioural outcomes.
Results
From 2908 articles identified in the initial search, 18 papers met the inclusion criteria. One further study was identified from the reference list search of included papers, resulting in a total of 19 included studies. Of 13 studies assessing cognitive function, 52.9% of children presented with intellectual disability or developmental delay. Among six papers reporting a formal assessment of ASD, 81 of 215 (37.7%) children had a diagnosis of ASD or a clinical level of symptoms. Five studies reported difficulties across emotional, social, and adaptive behavioural functioning. Heterogeneity of the neurobehavioural assessments used in these studies limited the evaluation of comparative outcomes.
Conclusions
Overall, the majority of studies suggest that children with SOD experience varied neurobehavioural impairments. Clinicians should therefore consider formal ASD and neurobehavioural assessments alongside routine care. There is, however, a need for more research specifically assessing behavioural, social, and emotional dysfunction, using sensitive and standardised tools in order to provide a more accurate estimate of these impairments in children with SOD.

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P44

Understanding the molecular basis of short stature in six patients with pathogenic variants in HMGA2

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Background
Silver-Russell syndrome (SRS) is a unique disorder characterised by characteristic features and growth restriction due to 11p15 LOM or upd(7)Mat in ~60% cases. Monogenic defects are a rare cause of SRS and *HMGA2* mutations have been identified in 4 cases to date. The function of *HMGA2* is poorly understood.
Objectives
Assess the clinical phenotypes of 6 new patients with novel heterozygous *HMGA2* defects and evaluate the molecular impact of the variants.
Methods
Pathogenicity prediction was conducted using a combination of computational platforms (SIFT, PolyPhen-2, Mutation Taster). Single nucleotide substitutions were generated by mutagenesis of an N-terminal FLAG tagged-HMGA2 cDNA. Frameshift constructs were customized to recapitulate reading frame extensions and generation of prolonged proteins. The variants were expressed in HEK293T cells and HMGA2 expression/nuclear localisation were assessed by immunoblotting whole cell lysates and nuclear/cytoplasmic fractions. Nuclear translocation of wild type and variant constructs were examined by confocal microscopy.
Results
Six patients from the UK, Netherlands and Mexico with variable height SDS (range -3.2 to -3.9) and IGF-I SDS (range from -1.9 to $+4.4$) were found to have deleterious variants in *HMGA2* with differing functional impacts: c.49G$>$T and c.52C$>$T stop gain variants leading to the introduction of a premature stop codon/early truncations, c.166A$>$G a missense variant predicted to alter the DNA binding domain and c.144delC, c.145delA and c.299dup frameshift variants leading to the generation of prolonged proteins. Phenotypic features were highly variable with little genotype-phenotype correlation. Expression of variant constructs in mammalian cells revealed detectable HMGA2 protein for all variants except the 2 truncations. Immunoblotting of nuclear fractions showed markedly reduced HMGA2 with the exception of c.166A$>$G, which demonstrated a subtle reduction. These findings were recapitulated by immunofluorescence.
Conclusions
We report a series of six patients with novel pathogenic variants in *HMGA2*. These cases presented with short stature and a spectrum of clinical features revealing the wide phenotypic, biochemical and genetic landscape of this rare syndrome. Functional characterisation revealed abnormal protein expression and nuclear localisation providing novel insights into the molecular basis of SRS pathogenesis.

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P45

The use of 6-monthly GnRH analogues in the paediatric population

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Background
Pubertal progression is inhibited in central precocious puberty with the use of gonadotropin releasing hormone (GnRH) analogues. They are usually given every 10 to 12 weeks via an intramuscular depot, but more recently, a 6-monthly preparation has become available for clinical use.
Aim
The aim of this project was to evaluate the efficacy and acceptability of 6-monthly triptorelin, a GnRH analogue, at a tertiary children's hospital.
Methods
Individuals who were receiving 12-weekly triptorelin or were due to start GnRH analogue therapy were offered the 6-monthly preparation (Decapeptyl SR 22.5 mg). Clinical data was collected on the patients who have received 6-monthly triptorelin.
Results
In total, 34 patients were identified with a mean age of 7.4 years ($+$ 1.4SD; range: 2-9) at diagnosis. 32/34 (94%) patients were female. All patients received the medication for central precocious puberty and the triptorelin was switched from 12-weekly formulation to 6-monthly at an average age of 8.1 years ($+$1.6SD; range: 2-10). 61.8% of patients have received two doses of the 6-monthly medication to date, with the remaining 38.2% having had one dose. 44.1% of patients have been

reviewed since commencing 6-monthly triptorelin and no progression in puberty has been noted. The injections have been tolerated well, with no side effects noted. The patient feedback has been positive with the need for less frequent injections and visits to the hospital.

Conclusion

The results have shown that over a short-term course, 6-monthly triptorelin has been well tolerated and has been effective in inhibiting pubertal progression. Long-term data is required, but these results are promising. The 6-monthly preparation has the potential to reduce the costs and the burden on limited healthcare resources.

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P46

A rare heterozygous *IGFI* variant impairing IGF-I cleavage and causing postnatal growth failure: a novel disease mechanism offering insights into IGF-I physiology

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Background

Pathogenic *IGFI* gene mutations causing childhood growth failure are extremely rare. Only five autosomal recessive mutations, one *IGFI* copy number variant and two heterozygous frameshift mutations are reported. Heterozygous missense *IGFI* mutations haven't previously been described.

Objectives

To identify and functionally characterise a novel missense *IGFI* variant in a patient with postnatal growth failure and delayed bone age.

Patient and Methods

The patient had a normal birth weight (-0.2 SDS) but height -3.4 SDS and head circumference -1.6 SDS by 10.1 years. Bone age was delayed by 2.5 years. A high peak GH was observed upon glucagon stimulation (17.1mcg/L). Baseline IGF-I levels were low/normal (144micrograms/L; -1.3 SDS) and responded poorly (increase <15micrograms/L) during IGF-I generation testing. Patient DNA was sequenced on our unique short stature gene panel. Functional analysis was performed using immunocytochemistry and furin cleavage assays. HEK293T cells transfected with *wildtype* and mutant *IGFI* constructs containing FLAG and HA tags were assessed by confocal microscopy. Whole cell lysates from HEK293T cells transfected with streptomycin-tagged *wildtype* and mutant *IGFI* constructs were incubated with furin to assess cleavage at the target site. *IGFI* constructs designed for the furin assay lacked the signal peptide, preventing their secretion from the cell and enabling them to be harvested from the cell lysate.

Results

We identified a rare novel heterozygous *IGFI* variant (102813333C>T, c.356G>A, p.R119H; gnoMAD frequency 0.004%) which was predicted damaging by SIFT; CADD score 32. This variant alters the first amino acid of IGF-I E domain, the most critical residue for furin binding, which is highly conserved across species. Furin cleaves pro-IGF-I to mature IGF-I (E domain removal). Functional analysis showed that both *wildtype* and mutant IGF-1 are able to translocate to the endoplasmic reticulum. Furin cleavage assay showed reduced cleavage for mutant p.R119H IGF-I compared to *wildtype*.

Conclusions

We report the first missense variant identified at the critical furin cleavage site, impairing the cleavage of pro-IGF-I to mature IGF-I. Our findings suggest the novel variant impairs pro-IGF-I cleavage, reducing mature circulating IGF-I levels. Pro-IGF-I is likely less biologically active than mature IGF-I, resulting in functional IGF-I deficiency and postnatal growth failure.

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Adrenal 2

P47

Salivary sampling in neonates, infants, and young children: glucocorticoid stability under different conditions and the introduction of a novel collection technique

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Background

Measurement of salivary glucocorticoids is gaining popularity as it offers a non-invasive collection technique, enabling sampling in the community or home environment, allowing tailored capture of steroid circadian rhythm and improved patient experience. Current popular salivary collection methods cannot be used in very young children due to choking and the requirement for active participation. There is little data on saliva stability during home collection.

Objectives

To compare salivary glucocorticoids sampled using different collection techniques; assess the salivary glucocorticoids stability under different storage conditions; evaluate time taken for salivary glucocorticoid collection and assess caregiver acceptability comparing the SalivaBio and a new salivary collection device designed for infants and young children – the SaliPacä (SalivaBio swab encased in an infant pacifier).

Methods

To compare devices, six healthy adults collected saliva samples using Salivette Cortisol®, passive drool and SalivaBio on retiring for bed, awakening and 3pm for five days. In the stability study volunteers provided saliva stored on SalivaBio swabs at 4°C, room temperature or 50°C for 24, 48, 72 hours or one week, replicating potential postage conditions. Salivary cortisol and cortisone concentrations were measured by LCMS. The SalivaBio and SaliPac feasibility study compared time to collect 1 ml of saliva and caregiver acceptability in 30 children <6yrs.

Results

There was no difference in salivary glucocorticoid concentrations collected using the three different methods. Salivary cortisol & cortisone were stable for 72 hours at room temperature and 4oC, with cortisone stable at 4°C and cortisol at room temperature out to a week. High temperature accelerated degradation. Repeated freeze-thaw cycles did not cause significant degradation. In children <6yrs the SalivaBio & SaliPac were well tolerated and collected sufficient saliva for salivary steroid analysis in under four minutes with no significant difference in collection time. There was a high level of acceptability in caregivers, who felt confident they could perform successful salivary collection at home using the SalivBio or SaliPac.

Conclusions

Salivette, passive drool and SalivaBio collect salivary samples with comparable cortisol & cortisone concentrations, which are stable under conditions that replicate home collection. Our novel SaliPac is an acceptable device for salivary sampling in young children.

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P48

Phenotypic variability in X-linked adrenoleukodystrophy

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Introduction

X-linked adrenoleukodystrophy (X-ALD) is due to mutation in ABCD1 with variable clinical phenotype and severity. Elevated plasma VLCFA is seen in all affected males. However, the clinical phenotype is not collated with VLCFA plasma concentration or by the type of ABCD1 variant. Clinical presentation can be widely variable ranging from childhood cerebral adrenoleukodystrophy (CALD), adolescent CALD, adrenomyloneuropathy and/or adrenal insufficiency. We present a series of patients with X-ALD due to ABCD1 mutation with varying clinical presentation.

Case history

Index patient from the first family presented at the age of 8.5 years with behavioural problems, and rapid neurological deterioration, and MRI brain was typical of X-LAD with Loes score of 15. The genetic testing confirmed maternally inherited ABCD1 splicing variant. His ACTH was elevated with suboptimal cortisol to synacthen test, and he was started on hydrocortisone treatment. His electrolytes were normal with normal renin and aldosterone. Unfortunately, due to his advanced MRI changes, he could not be offered haematopoietic stem cell transplant (HSCT). His 4-year-old and 11-year-old brothers were investigated and found to have elevated VLCFA with primary adrenal insufficiency and started on hydrocortisone therapy and the electrolytes, renin and aldosterone and MRI brain were normal. The fourth patient from another family was identified with ABCD1 mutation at the age of 10 months due to a strong family history of X-ALD. He was noted to have glucocorticoid deficiency with preserved neurological function. Several of his uncles had been diagnosed with X-ALD and needed only hydrocortisone and some developed neurological dysfunction later in the adulthood. One of his family members was also identified with gonadal failure at the age of 18 years needing testosterone treatment.

Discussion
Due to the deposition of VLCFA predominantly in the zona fasciculata of adrenal cortex, glucocorticoid deficiency is a consistent feature in these patients with spared mineralocorticoid at presentation. However, regular monitoring of electrolytes and plasma renin activity will be essential to identify evolving mineralocorticoid deficiency. Due to the deposition of VLCFA in the gonads, primary testicular failure could be a feature of X-ALD.

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Effect of high-dose maternal steroids on neonatal adrenal function

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Background
Limited data support concerns that corticosteroid use in pregnancy, for maternal health reasons, can suppress the neonatal Hypothalamic-Pituitary-Adrenal (HPA) axis. We sought to determine if neonates born to mothers on high-dose steroids are at risk of adrenal suppression.
Methodology
Our tertiary neonatal unit guidance advises that babies born to mothers receiving $\geq$7.5 mg/day prednisolone for 28 consecutive days in the 3rd trimester undergo HPA-axis assessment. Prior to 2019, three cortisol samples taken eight hours apart on day three of life were advised (group-1). Since 2019, guidance recommends a standard-dose synacthen test (SST) after 24hours of age (group-2). Neonates who underwent HPA-axis assessment over seven years (July 2014-June 2021) were identified from laboratory records. Demographic data; maternal steroid formulation, dose and duration; and outcome of HPA-axis assessment were collated through retrospective case note review. We defined a normal SST as a peak cortisol $>$500nmol/l prior to April 2016 and $>$430nmol/l from April 2016, due to a change in assay. For group-1 normal cortisol was defined as two cortisol levels $>$100nmol/l or one $>$200nmol/l. Neonates not meeting this threshold required further investigation with SST.
Results
Over the study period, 56 neonates underwent HPA-axis assessment due to maternal steroid use in pregnancy. The steroid equivalent dose of prednisolone prescribed was 5 mg-40 mg, and duration ranged from one month to throughout the pregnancy. Thirty-four babies underwent an SST; (Group-1 = 16, group-2 = 18). All neonates requiring a SST in group-1 demonstrated a normal response. Three neonates in group-2 had a suboptimal response (peak cortisol 318-348nmol/l) and were managed with "sick day rule' hydrocortisone. Mother-1 received 20 mg/day IV hydrocortisone for 3 weeks and 4 weeks of 5 mg/day prednisolone. Mother-2 received 20 mg/day prednisolone for 8 weeks. Steroid data were unavailable for mother-3. Baby-1 and 3 had a normal repeat SST after 6 weeks, baby-2 was lost to follow up.
Conclusions
The majority of babies born to mothers receiving corticosteroids during pregnancy do not have HPA-axis suppression. However, some neonates may be at risk of transient adrenal suppression. Further studies focusing on normal neonatal adrenal function and steroid use in pregnancy are needed to guide when HPA-axis assessment may be required.

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P50

Safety alerts for patients at high risk of acute adrenal insufficiency

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Background
Acute adrenal insufficiency is a medical emergency and patients at risk of adrenal crisis should be treated immediately with glucocorticoid replacement. Our aim was to ensure there were safety alerts in place for health care professionals managing steroid dependent patients, to highlight their risk of adrenal insufficiency, and therefore prevent delays in life saving treatment.
Methods
Review of the electronic documentation of all the steroid dependent Paediatric patients at the Royal United Hospital, Bath, for a safety alert highlighting their risk of adrenal insufficiency. Review of the alerts in place with the local ambulance service on the same population of steroid dependent Paediatric patients. Created an alert on high-risk Paediatric patients' notes, flagging their risk of adrenal insufficiency. Developed a safety alert pop-up box, which must be physically acknowledged, to appear every time the patients' notes are accessed. Formed a check list for all newly diagnosed steroid dependent patients, who are at risk of adrenal insufficiency, to ensure the appropriate alerts are created on diagnosis.
Results
95% of Paediatric patients on steroid replacement therapy did not have an alert on their electronic documentation stating they were at high risk of adrenal insufficiency. 10% of these patients also did not have an alert with the local ambulance service highlighting their steroid dependence and risk of adrenal insufficiency. 100% of the steroid dependent Paediatric patients now have an alert on their electronic documentation and with the local ambulance service. This will be re-audited in 24 months to ensure the ongoing implementation of safety alerts for newly diagnosed steroid dependent Paediatric patients.
Conclusion:
Steroid dependent Paediatric patients at the Royal United Hospital, Bath, now have multiple safety alerts in place to ensure health care professionals are aware of their risk of acute adrenal insufficiency.

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P51

Paediatric adrenocortical carcinoma presents with virilization and glucocorticoid deficiency – a rare presentation

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Background
Adrenocortical carcinoma in childhood is a rare tumour which accounts for about 0.2% of all paediatric malignancies. Affected children usually present with virilization, cushingoid features, and/or mineralocorticoid excess. We present a boy with adrenal carcinoma presented with virilization and unusually suppressed cortisol at initial presentation.
Case report
A two-year-old boy presented with pubic hair, acne, and increased penile growth without cushingoid features for three months. He was normotensive and his abdominal examination was free of distinctive abdominal masses. His hormonal evaluation revealed raised DHEAS (140µg/dl) and testosterone (6.45nmol/l). He had low random serum cortisol with suppressed cortisol response to the Synacthen test (peak cortisol 95nmol/l). His 17α Hydroxyprogesterone and ACTH were normal. Alpha-fetoprotein (αFP) and βHCG were normal. His bone age was advanced by one year. There was no mediastinal mass in the chest X-ray and abdominal ultrasonography (USS) excluded adrenal or liver masses. Urinary steroid profile was not done due to unavailability. He was started on hydrocortisone replacement and closely followed up. After six months, he developed cushingoid features along with rapid virilization and hypertension. Re-evaluation of the hormonal analysis revealed markedly elevated DHEAS (1007µg/dl), cortisol ($>$1000nmol/l) and suppressed ACTH (1.2pg/ml). Dexamethasone suppression test failed to suppress cortisol. Repeat USS and CT abdomen/chest revealed a left-sided adrenal mass measuring 5.5$\times$5. 1$\times$8 cm without distance metastasis. He underwent left-sided adrenalectomy along with a nephrectomy without postoperative complications. Histology of the tissue sample revealed adrenocortical carcinoma with nodal tumour deposit at the renal hilum. He was started on adjunct treatment with mitotane along with hydrocortisone and fludrocortisone maintenance therapy. After 6 months, the child was clinically well with normal DHEAS. His repeat CT abdominal scan at 6 months was normal without tumour recurrence.
Conclusion
This case highlights the rare initial presentation of an adrenal carcinoma with suppressed cortisol levels. The mechanism of suppressed cortisol in adrenal carcinoma in this child was unclear. A high index of clinical suspicion guided regular clinical, biochemical and radiological monitoring helped with early diagnosis and treatment in a resource-limited country.

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Diabetes 2

P52

Review of glycaemic control following change from standardised insulin pump to hybrid closed loop

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Introduction
Hybrid closed loop pumps (HCL) incorporate insulin pumps (IPs) with continuous glucose monitoring (CGM). Basal and bolus insulin release can be algorithmically adjusted in real-time enabling some automated insulin changes between meals according to set parameters. We reviewed the glycaemic control of patients with T1D cared for at the Evelina who had upgraded from IP to HCL between October 2020 and January 2022.
Methods
As per standard care, patients were reviewed in clinic every 3 months and HbA1c was measured, and time in range (TIR) reviewed using CGM data. In between visits pump downloads were reviewed to optimise IP settings. Patients selected were upgraded when they were eligible for a new pump (pump warranty is 4 years) if they wished to embrace the new technology. When upgrading, patients and their parents/carers were instructed on HCL use by a diabetes professional.
Results
Overall, 13 patients had been upgraded, from which 9 (6 male) fell within the date range and had sufficient data for analysis. Median age was 10 years (range, 6-16). Mean HbA1c values were calculated for each patient before and after upgrade and TIR reviewed. The mean HbA1c of the group before HCL was 7.640% (60 mmol/mol), SD +/-0.484%, and after HCL was 6.919% (52 mmol/mol), SD +/- 0.244%. A single-tailed paired t-test was used to compare the HbA1c values, giving a t-value of 3.99 (16 DoF), showing a P-value of <0.0003. Mean time in range (TIR) was calculated before upgrade 53.5%, SD +/-10.94% and afterwards 68%, SD +/-7.34%, with a P-value of 0.0019.
Conclusions
Our review shows a significant improvement in glycaemic control following a switch from a simple IP to a HCL in our paediatric patients with T1D. Of note these patients had reasonable diabetes control before the switch but were able to make significant improvements having made the switch. However this is a small sample size, and so should be investigated further with a larger sample, ideally incorporating some quality of life data.

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P53

Diabetic ketoacidosis in children and young people (CYP) at diagnosis across Wales during the COVID-19 pandemic: have the quality improvement (QI) innovations made an impact?

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Introduction
There were concerns voiced by health care professionals (HCPs) that restrictions to healthcare delivery during the pandemic has resulted in delays in diagnosing T1D in CYP. Most CYP present with symptoms of T1D to primary care. Delay in diagnosis increases the risk of potentially life-threatening diabetic ketoacidosis (DKA). In Cardiff, we piloted QI initiatives pre-pandemic to improve early diagnosis which was introduced across the Children and Young People's Wales Diabetes Network (CYPWDN). Early in the pandemic, we escalated responses to facilitate early diagnosis.
Objectives
To analyse the impact of the QI initiatives during the pandemic on the incidence of DKA at diagnosis across Wales. The primary objective being to develop effective pathways to facilitate early diagnosis and prevent DKA.
Methods
Data over four years from the Brecon Registry of all newly diagnosed CYP in Wales was analysed; pre-pandemic (01/04/18 – 31/03/20), pandemic (01/04/20 – 31/03/22). Key points included age at diagnosis, mortality, pH, bicarbonate and health board. At the start of the pandemic, we identified barriers facing HCPs in primary care, 111, Welsh ambulance service and developed initiatives to improve timely diagnosis. This included an updated referral pathway, triage tools/algorithms and continued feedback.
Results
There has been a 22% increase in new T1D diagnoses ($n=322$ to $n=394$). DKA incidence has increased from 31% to 35%. There was a significant increase in the severity of DKA to more than double that of the pre-pandemic period. We had one mortality due to undiagnosed T1D at the start of the pandemic. 2 of the 6 health boards who actively implemented the QI tools maintained the same DKA incidence and demonstrated a reduction in those presenting in severe DKA across the 4 years.
Conclusions
There has been a significant increase in CYP presenting in severe DKA at diagnosis in Wales. Although there was no significant reduction in overall DKA rates, two health boards have demonstrated improvement following QI initiatives between primary and secondary care. This QI programme should be implemented across other parts of Wales with a long-term plan to promote early diagnosis and reduce the incidence of DKA at diagnosis.

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P54

Technology alone is not the answer for closing the deprivation gap in Type 1 Diabetes Mellitus (T1DM)

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Introduction
Children and young people with T1DM living in the least deprived areas have better diabetes control vs those in most deprived areas with UK NPDA data suggesting that deprivation and ethnicity are associated with less use of technology.[1]
Aims
1. Review distribution of technology between different socio-economic and ethnic groups 2. To compare mean recent HbA1c results between groups using different combinations of technology
Method
Using databases (EPR and Twinkle) we obtained data on all T1DM patients under Wythenshawe Hospital. An IMD deprivation score was generated using postcode (English indices of deprivation 2019) and converted into deciles. We used regression modelling to analyse the relationship between technology, deprivation, demographics and HbA1c.
Results
142 patients were reviewed with 47.9% using insulin pumps, 46.5% using multiple daily injections (MDI) with continuous glucose monitoring (CGM) and 5.6% using MDI and finger-prick testing. For HbA1c comparison we used 52 patients on pumps (16 excluded) and 65 patients injections (9 excluded). Our population had similar proportions of ethnic groups, compared to nationally, however it is more skewed to the extremes of social deprivation. There was similar use of diabetes technology across all ethnic and socio-economic groups. There was less use of insulin pumps in the Black ethnicity group ($n=6$). HbA1c results were significantly higher in the most deprived compared with the least deprived areas. For each increasing decile of IMD, HBA1c is 0.75 mmol/mol lower (95%CI -1.48 - -0.02) $P=0.045$. There was no significant difference between closed loop and non-closed loop pump systems b = 2.16 (95%CI -3.13 – 7.46) $P=0.415$. For patients on MDI, there was no significant difference between finger-prick testing and CGM. Insulin pumps were associated with an HbA1c 9.57 mmol/mol lower (95%CI 4.41- 14.73) ($P=<0.001$).
Conclusion
Despite even distribution of technology between socioeconomic groups increasing levels of deprivation were associated with worsening glycaemic control. Further work should include looking at more detailed data to assess use of technology (e.g time in range, percentage sensor use) and to collect qualitative data on patient's experience.
References
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P55

Recognising and raising safeguarding and child protection issues in childrens diabetes. Early findings from a qualitative study exploring specialist paediatric diabetes healthcare professionals' experiences

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Introduction
Managing diabetes in a child is complex and demanding for parents, for some families this is exacerbated by additional demands. Compromised family capacity may lead to diminished management of a child's diabetes, increasing the risk for acute and long-term complications. The UK has the highest rates in Europe of children (0-14years) living with Type 1 diabetes (International Diabetes Federation, 2019) however, it is concerning that less than 40% have a HbA1c less than 58 mmol/mol (HQIP, 2022). Where health care professional's (HCPs) recommendations for children with health problems are not integrated into day to day care, neglect is increasingly considered (Dubowitz, 2011). However, the absence of frank signs of maltreatment and therefore, evidencing concerns presents challenges. Specialist children's diabetes HCPs experiences of negotiating these multiplex situations have not yet been explored
Methods
This qualitative study analyses data from semi-structured interviews using grounded theory methodology. It explores HCP's experiences of working with children where families care of diabetes is compromised. It aims to develop an understanding of how professionals recognise safeguarding issues and determine factors contributing to and influencing raising their safeguarding concerns.
Findings
Early findings suggest factors influencing concerns are complex and multifaceted and challenging for professionals. HCPs describe difficulty identifying child maltreatment, demonstrating the use of intricate skills to develop and understand concerns including, for some, intuition. Further difficulties arise in the absence of joint risk language as HCPs present frustrations communicating effectively between services. Participants confer common anxieties and challenges including managing risk where thresholds for intervention are not met, as well as feeling that they are holding responsibility for families. Participants report that despite recognition of the benefits of sharing practice and working together, this is limited, both within their own diabetes teams and across other agencies. Recommendations for practice include enriched professional development to include improving referrals and multiagency collaboration, alongside managing the physical and emotional demands of safeguarding.
Conclusions
Further exploration is required to understand diabetes professionals' appraisal, and use of, less tangible signs to identify neglect early, and also how child abuse and maltreatment is managed within teams

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P56

Improving early diagnosis of type 1 diabetes (T1D) during the COVID-19 pandemic

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Introduction
The pandemic resulted in changes in delivery of healthcare. Most children and young people (CYP) present with symptoms of T1D for the first time to primary care. Delayed diagnosis is common and associated with risk of life-threatening diabetic ketoacidosis (DKA). In Cardiff, we had a pre-pandemic QI project to improve early diagnosis of T1D. We escalated responses, introduced initiatives to facilitate early diagnosis.
Aim
To develop effective pathways to facilitate early diagnosis of T1D during the pandemic.
Methods
At the start of the pandemic, we identified barriers facing healthcare professionals (HCPs) in primary care, 111, Welsh ambulance service and developed initiatives to improve timely diagnosis. This included an updated referral pathway, triage tools/algorithms and continued feedback. We raised public awareness through school social media and health board channels. Two audit cycles over four years: Retrospective case note analysis of all newly diagnosed CYP in Cardiff; pre-pandemic (01/04/18 – 31/03/20), pandemic (01/04/20 – 31/03/22). Key points included delayed diagnosis, presentation, appropriate testing and referral.
Results
Pre-pandemic: Most children presented to primary care, 7 had delayed diagnosis, 6/7 were due to triage delays, 1 had fasting blood glucose test resulting in delay. Pandemic: An increase in the number newly diagnosed, 4 had delayed diagnosis, 2 due to delayed triage. The 4 in severe DKA were delayed presentations to HCPs and promptly diagnosed, 2 were assumed to have COVID symptoms. During the pandemic 91% had POC testing and prompt referral in comparison to 75% pre-pandemic. There was no increase in DKA rates during the pandemic.
Conclusions
During the COVID-19 pandemic, we demonstrated an improvement in prompt diagnosis of T1D in Cardiff following collaborative working between primary and secondary care. Delayed presentation resulted in severe DKA despite public awareness campaigns. Data analysis, feedback, training across Wales is planned with a long-term objective to reduce the incidence of DKA at diagnosis.

	PRE-PANDEMIC	PANDEMIC
Total T1D Diagnoses	40	60
DKA at diagnoses	12 (30%)	17 (28.3%)
Diagnosed in Primary Care	31	42
Incident forms	3	3
Delayed diagnosis	7	4
Delayed presentation	6	12
DKA Severity		
Mild	5	10
Moderate	6	3
Severe	1	4

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P57

Compliance with screening and monitoring guidelines for macrovascular cardiovascular disease in children and young people with diabetes

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Background
NICE guidance (NG18) and East & North Hertfordshire NHS Trust (ENHT) CG048 recommend that in order to prevent macrovascular cardiovascular disease, services for Children and Young People with Diabetes (CYPD) offer monitoring annually from 12 years for microalbuminuria (to detect diabetic kidney disease), hypertension and dyslipidaemia. Anecdotally, elevated blood pressure (BP) readings in clinic were often attributed to anxiety or an incorrect cuff size and were therefore rarely actioned.
Method
We conducted a retrospective audit identifying 109 patients on the ENHT CYPD patient list, aged 12-16 years in December 2021, who had at least 1 annual review following diagnosis. We sampled 41 of these patients and reviewed the Clinical Information and Patient Tracking System (CIPTS) and Integrated Clinical Environment (ICE) results system. 3 patients were excluded as they had not attended a diabetic annual review after their 12th birthday (1/41) or in the previous 18 months (2/41), leaving 38 patients.
Results
Annual monitoring for microalbuminuria was recorded for 76.3% of patients, 17.2% (5/29) had an elevated albumin creatinine ratio (ACR) of 3-30 mg/mmol. Annual blood pressure measurements had been recorded for all patients, 39.5% had consistently elevated BP readings (systolic >120mmHg in ≥ 3 of 4 most recent reviews). Annual monitoring for dyslipidaemia had been undertaken for 68.4% of patients, 80.8% (21/26) had total cholesterol levels ≥ 4.0 mmol/l at their most recent annual review. No evidence of further investigation, monitoring, diagnosis, treatment or referral to a tertiary centre was identified for patients with abnormal results in our sample.
Conclusion
All patients had annual BP measurements, however fewer provided urine or blood samples. Logistical and psychological factors contribute to reduced uptake of screening. There was no documentation to indicate abnormal results had been actioned. We presented these findings at our diabetes multidisciplinary team meeting, and will encourage manual BP training for clinical staff and a flowchart to prompt actioning of abnormal BP readings. We intend to automate recall for abnormal biochemistry results and simplify our referral process to tertiary care. We are implementing a system of continual assessment of these measures to track progressive change as our proposals are enacted.

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P58

COVID-19 and newly diagnosed type1 diabetes mellitus in paediatrics

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Keywords: COVID-19, Diabetes Mellitus, Paediatrics
Introduction
COVID-19 has a complex relationship with diabetes. There is anecdotal evidence that it could be causative for new onset diabetes in paediatrics. In this audit, we

aim to study our cohort of new onset diabetes in children and young people (CYP) during the COVID pandemic in a DGH setting. We sought to identify any causative or associational link between COVID-19 and new onset diabetes.
Method
We reviewed the hand written notes, e-notes and investigations available on the pathology server for our newly diagnosed diabetes CYP from February 2020 to January 2022. We compared the number of new diagnosis and DKA presentation, with the previous two years (April 2018 till Jan 2020), which was pre-COVID.
Results
A total of 65 cases were included in this audit, of which 39 boys and 26 girls. Age ranged from 9 months to 17 years. 47 were White British. The most common presenting symptoms was polyuria followed by polydipsia and weight loss. 55% of patient presented to the hospital within three weeks of the beginning of their symptoms. 40% of patients were in DKA at presentation. GAD and/or IA2 antibodies were presented in 60 (90%) cases. Only four patients were positive for COVID-19, 40 cases were negative at the time of presentation and the rest were not tested. In comparison to the two years pre-COVID, the newly diagnosed type1 diabetes cases number increased by 25%. DKA at presentation in this time increased by 3%, and not attributed to delayed presentation.
Conclusion
We have demonstrated a 25% increase in new onset diabetes during the 2 years of pandemic, with a 3% increase in rate of DKA. 90% of the newly diagnosed CYP were autoantibody positive, hence had the immune predisposition. However, we have not been able to prove a direct link between COVID-19 infection and new onset diabetes in CYP. Hence is COVID-19 causative or associational, this question begs further studies.

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P59

An alternative case of diabetes

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Aims
To present a case of steroid induced diabetes and use this opportunity to review the diabetic resources we provide to other speciality teams in our hospital.
Case
A fifteen year old patient was diagnosed with acute lymphoblastic leukaemia from a full blood count and bone marrow biopsy following a short history of lymph node swelling. He was started on a treatment regime that included dexamethasone at a dose of 6 mg/m^2. Later that week the endocrine team were asked to review after random blood sugars of up to 18.6 and a fasting sugar of 13.4 was noted in the previous 24 hours along with glucose in the urine dip. Ketones had been checked and were low throughout. He did not complain of any osmotic symptoms. We based his total daily dose (TDD) of insulin on both on his pre-theatre sliding scale (he was fasting at the time of diagnosis) and ACDC guidance[1]. He was then commenced on a set dose regime of novorapid and tresiba with calculated correction factors. During the rest of his inpatient stay his management was reviewed daily and both he and his parents received education via the paediatric diabetic nursing team.
Follow up
Diabetic team reviews were provided at further haematology appointments and guidance given for pre-operative care. When steroids were due to be weaned off we provided a complimentary regime for the reduction of insulin until both were stopped. His blood sugars remained within the normal range thereafter.
Conclusions
Using ACDC and BSPED guidelines[1] we were able to manage this patient through his transient diabetes without complication. Following this case we have updated our hospital guidance on the management of pre-operative diabetic patients and produced a quick reference guide on the identification and management of steroid induced diabetes.
References
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P60

A case of possible diabetes in remission in a 15 year old girl with significant deliberate weight loss

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Background
Type 1 diabetes (T1D) is a metabolic disease of unknown aetiology that results from the autoimmune destruction of the insulin-producing pancreatic β-cells. Exogenous insulin administration is the only treatment for patients. Partial remission or "honeymoon phase" classically occurs a few weeks after insulin therapy has been initiated. During this stage the patient's need for exogenous insulin can decline by 50%, and near-normal metabolic control is maintained. In a few cases, even temporary insulin independence can be achieved. Several clinical and metabolic factors have been found to influence the frequency and duration of the remission period, which depends partly on the recovery of β-cell function. The duration of this stage can vary from weeks to years. This stage of partial remission has generated much interest for the application of future therapies.
Case Report
14 year old female presented November 2022 with 6 week history; polyuria, polydipsia and weight loss. Initial presentation consistent with diabetes not in DKA. Blood glucose 23.4 mmol/l, Ketones 0.5 mmol/l. pH 7.4 on admission blood gas. Investigations; Pancreatic Islet Cell Antibodies - weak positive, Anti-GAD Antibodies - 23.4 U/ml (positive > 25U/ml), IgG Insulin Antibodies - 2.8 (0.0-5.0), HbA1c - 121 mmol/mol (< 48 mmol/mol), ZnT8 sample lost in transit. Commenced on SC insulin 1unit/kg/day combination novorapid and lantus. Achieved good glycaemic control and was followed up in clinic. Subsequently commenced on continuous insulin pump with excellent control. Further admission May 2022. History of deliberate weight loss (91-98th percentile to 50-75th) restrictive diet (100kcal/day) and recurrent hypoglycaemic episodes. During admission insulin cautiously weaned to zero. Post mixed meal identified presence of urinary C-peptide indicating exogenous insulin production. Patient has been off insulin since May 2022. Repeat autoimmune workup awaited. Ongoing Libra monitor - flat-line with occasional peak > 10 mmol. 90% in range.
Discussion
Is this a correct diagnosis of T1D? Unaware of antibody status. Could this be a case of prolonged honeymoon period secondary to deliberate weight loss? Could this be sustained honeymoon phase or even total remission? How could we monitor biomarkers in this phase that correlate with β-cell regeneration and immunotolerance induction? Can we predict; short term remission, intermediate remission or long term remission?

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Diabetes 3

P61

GAME-SET-MATCH mnemonic: an infographic to teach effective dynamic glucose management strategies improving time in range in children with type 1 diabetes using continuous glucose monitoring

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Background
Continuous Glucose Monitoring (CGM) is now becoming the standard of care for children and young people with diabetes (CYPD). Due to a lack of validated education programmes, we created 'The CGM Academy' delivering evidence-based structured education. The results of the first 50 CYPD graduating from the academy demonstrated statistically significant improvement in time in range (TIR, 3.9-10.0 mmol/l) by 8.3% ($P < 0.001$) and HbA1c by 3.8 mmol/mol ($P < 0.001$) when dynamic glucose management (dynamic GM) strategies were implemented. The subsequent analysis enabled the determination of the most effective strategies for the first 100 graduates and presentation in a user-friendly format avoiding fatigue.
Methods
Step 1) The first 100 CYPD CGM Academy graduates completed a questionnaire at six months documenting their use of the seven dynamic GM strategies:(1) Prevent hypos (2) Trend Arrow Adjustment Tool (TATT), (3) Bolus timing (4) Exercise checks (5) Regular CGM report review (6) Short bursts of exercise and (7) Insulin corrections. Step 2) Factors predicting TIR were identified after adjusting for variables, using multiple linear regression. Step 3) using the strongest predictors of TIR, an infographic was co-created by the diabetes team and CYPD.
Results
The best predictors for TIR were: Short bursts of exercise ($\beta = 3.261$, $P < 0.001$), Bolus timing ($\beta = 2.651$, $P = 0.006$), and Prevent hypos ($\beta = 2.52$, $P = 0.015$).

These three strategies were condensed into a mnemonic facilitating ease of teaching and memory retention: GAME (Stop highs)-SET (stay in target) - MATCH (Prevent lows). GAME: G = Glucose percentage TIR desired, A = Alert on high set accordingly, M = Mode of exercise, E = Exercise time. SET: S = Start insulin before eating, E = Eat three balanced meals, T = Ten minutes of moderate activity. MATCH: M = Measure weight in kilograms, A = Always use glucose, T = Try to prevent hypoglycaemia, C = Change glucose amount, H = Have patience and wait 20 minutes.

Conclusion

Teaching the most effective dynamic GM strategies avoids user overload and fatigue. The use of an infographic has eased the reiteration of taught strategies in the busy clinic setting. The retention of taught strategies will be further evaluated on an ongoing basis.

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P62

Recognition and management of hypertension in children and young people with diabetes

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Introduction

The NPDA presents data on management, treatment, and complications for all diabetes units in the country. This acts as a driver for quality improvement and aims to improve standards of diabetes care. The 2019 report identified a relatively high proportion of children with hypertension locally. An audit aimed to identify the proportion of local diabetes patients with 'hypertension' or 'pre-hypertension', and their clinical identification. The subsequent clinical management was then reviewed.

Methods

A local database for all patients over the age of 12 years with a diagnosis of diabetes was created. The following information was collected from each patient's most recent 4 clinic appointments; sex, age at appointment, duration of diabetes, height, height centile, blood pressure (BP), and BP centile. BP readings were categorised as normal (<90th centile), pre-hypertensive (90th > 95th centile), and hypertensive (≥95th centile). Clinical records were used to assess whether the clinician had correctly identified the presence of raised BP, along with subsequent investigations and treatment.

Results

BP readings from a total of 154 patients with diabetes were reviewed. All patients had their blood pressure measured at least annually. In total, 50/154 (32%) patients were found to have normal blood pressure, 7/154 (4%) had pre-hypertension and 42/154 (27%) had hypertension. The remaining 55/154 (36%) had mixed results. In over half of cases (63%), raised BP went unidentified by clinicians. Where raised BP was recognised, further assessment and investigation was variable. 8/18 patients had 24-hour BP monitoring requested, one performed home measurements, but 9 patients had no plan given by clinicians. Additional investigations were performed as part of an annual review with no evidence that investigations were specifically requested as a result of raised BP.

Conclusion

The Paediatric Diabetes Team supports the patient and family to optimise their diabetes management, whilst monitoring for and minimising the risk of the development of complications. Monitoring of BP occurs reliably, but clinician interpretation of measurements requires improvement. Standardisation of hypertension definitions and management would be a useful step in optimising the cardiovascular health of young patients with diabetes.

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P63

Audit of the use of HbA1c in children and young people without a prior diagnosis of diabetes mellitus

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Background

HbA1c is an important indicator of long-term glycaemic control in CYP with established diabetes mellitus (DM). The WHO recommends that diagnosis of DM requires measurement of blood glucose, and that HbA1c is not validated as a diagnostic test in CYP. NICE guidance recommends any child with suspected Type 1 DM should have a POC BG test and same day referral to secondary care. Requesting HbA1c in primary care may delay diagnosis of Type 1 DM, leading to potentially life threatening DKA at diagnosis.

Aims

To establish the number of children without a previous diagnosis of DM having HbA1c measured, along with the clinical indications and location of requesting clinicians, and establish the incidence of potentially delayed diagnoses of DM in this cohort.

Method

Retrospective data from the Biochemistry labs of all HbA1cs performed in children <16 years over a 2 year period was obtained, and the clinical portal documentation was reviewed and analysed.

Results

2122 HbA1cs were performed during the selected time period. 274 samples from patients with a previous diagnosis of DM and 36 samples from patients with Cystic Fibrosis undergoing annual review were excluded, leaving 1812 samples analysed. 1580 samples (87%) were from Primary care. Overall 94.3% of results were <42 mmol/mol. However, when analysed separately, 25% of HbA1cs from Secondary care were >48 mmol/mol, vs <1% in Primary care. Of those subsequently diagnosed with DM, five had a delayed diagnosis. No clinical indication was documented for 33.5% of samples. The most common stated clinical indication was lethargy. 51 patients from primary care, had clinical indication mentioning polydipsia or polyuria.

Conclusion

The majority of HbA1cs performed in primary care had no clear clinical indication. In addition, patients presenting with symptoms suggestive of Type 1 DM are having "routine bloods" arranged rather than POC glucose testing and referral to secondary care as per NICE guidance. We propose to limit this using a prompting algorithm in the electronic test requesting process for HbA1cs in under 16s, and work collaboratively with primary care in order to optimise use of resources and reduce patient risk.

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Protocol for a feasibility study and process evaluation of a psychosocially modelled diabetes education programme for young people with type 1 diabetes: the yes study

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Background

Adolescence is a challenging time for people with type 1 diabetes (T1DM), associated with worsening glycaemia and disengagement with care. Educational interventions often focus on imparting diabetes-specific skills rather than attending to some of the broader psychosocial challenges young people commonly experience. To address this, we codesigned a psychosocially modelled programme of diabetes education, named 'Youth Empowerment Skills' (YES), with young people with T1DM. The programme aims to facilitate a positive adaptation to life with diabetes and engagement with diabetes care through peer-based learning, immersive simulations and support from outreach youth workers. This programme has been running successfully in South London for five years, with positive feedback from young people who participated.

Aim

To test the feasibility (acceptability, implementability, recruitment and completion) of the YES programme, and estimate its efficacy in relation to metabolic (glycaeted haemoglobin), healthcare (emergency and hypoglycaemic events) and psychosocial (diabetes self-management, confidence in managing healthcare, illness perception and quality of life) outcomes.

Method

We will conduct a feasibility randomised controlled trial (waiting-list design) with integrated process evaluation in diabetes centres in London, UK, which serve socioculturally diverse populations. Fifty young people with T1DM (aged 14–19 years) will be randomly allocated to either the YES intervention or a waiting-list control. Randomisation acceptability will be assessed with provision for a preference allocation. Outcomes will be evaluated at 6 months, at which point the waiting list participants will be exposed to the YES programme with further follow-up to 12 months. A simultaneous process evaluation will use a mixed-methods approach collecting both qualitative and quantitative data from patients and providers to establish early implementability of YES.

Results
The study findings will be used together with a review event to optimise intervention components, outcome measures and recruitment methods to inform a subsequent definitive trial.
Conclusion
There is a need to develop and test new approaches for young people with T1DM that support them with the significant psychological and social challenges they experience. This study will help establish trial feasibility, indications of clinical effectiveness and implementation success factors of a co-designed psychosocially modelled intervention to support young people with T1DM.

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Use of artificial pancreas systems in routine clinical care is effective in improving glycaemic control in paediatric patients

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Introduction
Artificial pancreas systems (APS) have improved glycaemic control in adult and paediatric patients in clinical trials as part of routine clinical care
Aim and objectives
To evaluate the effectiveness of artificial pancreas system in routine clinical care on glycaemic control over a period of three to six months. Changes in glycated haemoglobin (HbA1c), time in range (TIR, 3.9-10 mmol/l) and time below range (TBR, <3.9 mmol/l) were assessed.
Methodology
Retrospective analysis of HbA1c, TIR, TBR in 42 paediatric patients using APS as part of routine clinical care between May 2020 to December 2021. Age group of these patient was 1 to 18 years with median being 11 years. Of 42 patients, 13 patients were on multiple daily injections (MDI) and 29 were on insulin pump before starting on APS. APS used were T slim Control IQ ($n=36$) and CamAPS FX ($n=6$). We retrieved patient data from cloud-based storage systems, Dexcom clarity and Diasend, for TIR and TBR, HbA1c was retrieved via electronical case notes. Only patients with minimum of one recorded HbA1c, TIR, TIHR reading pre and post APS were included. Exclusion criteria: transfer of care, use of continuous glucose monitoring less than 70% of total time, lack of data. Out of initial 42 patients using APS, 28 patients were eligible for HbA1C cohort, 35 for TIR cohort and 29 for TBR cohort, based on inclusion and exclusion criteria.
Results
Baseline mean HbA1c was 62.4 mmol/mol (range 51.6-78.3) and improved to 56 mmol/mol (range 49-71.5) at three months and 56.5 mmol/mol (range 48-81) at six months (improvement: -9.45 %; $P<0.05$). TIR improved from 49.69% (range 14-76) at baseline to 60.60% (range 35-77) at three months and remained at 59.33% (range 33.6-76.1) at 6 months. (Improvement: - TBR at baseline was 2.69% (range 0.6-11.6), 1.91% (range 0-8.3) at three months and 2.15% (range 0.2-8.3) at six months (improvement by 20.7%; $P<0.05$)
Conclusion
Our data demonstrate that the use of APS in routine clinical care leads to sustained improvement in glycaemic control including children. Further evaluation is required to understand not just the medical, but also the psychological benefits for children and families

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Simplified diabetes education for parents with poor health literacy

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Diabetes mellitus education for children, young people and their families has become more complex in recent years, requiring a solid knowledge of mathematics, problem solving and ongoing adjustments as the child grows. The education at time of diagnosis can be overwhelming for many parents who are coming to terms with this lifelong condition. But we, as diabetes teams also expect them to take on new and alien tasks, not only blood glucose testing and injecting insulin, but also understanding nutritional labels, calculating carbohydrates in meals and determining a safe dose of a very potent drug. All this whilst their child grows and develops frequently changing the goal posts. This is daunting for the best of us but can be hugely challenging for parents who struggled educationally and were glad to leave their school days behind them. The Belfast Trust is situated in an area of increased economic and social deprivation, and with the legacy of 'the troubles', has a high percentage of parents who have limited education and health literacy. We frequently encounter parents who cannot grasp the various aspects of the daily management of their child's diabetes, despite the best efforts of the team. We realised we needed to adapt the general education tools we had available, with increased 'one to one' teaching and simplifying our educational material. The CHOICE team, who provide structured education in CHO counting, tailored their teaching specifically for these parents. We focused on giving simple, clear and direct instructions to manage their child's condition, for example hypoglycaemic treatment and sick day rules. We also introduced an interactive educational tool called DEAAP; which provides short, colourful and engaging diabetes educational cartoons. The parents can download this app on to their phone for continued learning at their own pace. This kit also includes interactive teaching aids, helping to address all methods of learning. The education is provided mainly by the nurses and dietitians, who continually gauge parental understanding throughout education sessions and adapt resources to make the learning appropriate for each family.

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Prolonged honeymoon phase in 2 paediatric cases with type 1 diabetes mellitus

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Introduction
At the onset of type 1 diabetes mellitus (T1DM), children often experience a partial remission which is characterized by decreased insulin requirements. Usually, some exogenous insulin is still needed during this honeymoon phase. We present cases of 2 children with T1DM who had significantly extended periods where no exogenous insulin was required. Case 1: 12-year-old girl presented with fatigue and weight gain. HbA1c in primary care was 51 mmol/mol. BMI was +3 SD. She made immediate significant changes in diet and physical activity. Continuous glucose monitoring one week later showed time in range of 92% without any medication. GAD antibodies were strongly positive. Lifestyle changes were maintained, BMI fell to 98th centile, and HbA1c dropped to 31 mmol/mol, remaining normal for 2 years. Working diagnosis was possible type 2 diabetes mellitus and she was monitored 3 monthly in diabetes clinic. 2 years later she developed osmotic symptoms after a period of increased snacking and reduced blood glucose testing. HbA1c was 92 mmol/mol and blood glucose 19 mmol/l. She was commenced on multiple daily dose insulin. Within 4 months her HbA1c reduced to 29 mmol/mol with 95% time in range. Case 2: 12-year-old boy presented with lethargy, weight loss and nocturia. Blood glucose was 18 mmol/l, ketones 5 mmol/l, pH 7.29, HbA1c 99 mmol/mol. IA-2 antibodies were strongly positive. He was started on multiple daily dose insulin. He followed a healthy diet with low snacking and exercised regularly. Insulin was stopped after 2-3 weeks due to hypoglycaemia. Over the next 15 months HbA1c was maintained at 35-37 mmol/mol without insulin. 17 months after the initial diagnosis blood glucose levels began to rise and he was restarted on insulin injections. HbA1c at resumption of insulin injections was 43 mmol/mol.
Conclusion
Extended honeymoon phase can be seen in children with diabetes. Common characteristics of our patients were healthy diet with low snacking, regular exercise, and in one case significant weight loss. Careful communication with families to ensure good understanding of the honeymoon phase is important, including regular blood glucose monitoring to detect changes early.

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Insulin adjustment for local cultural event (summer marching season)

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In Northern Ireland the annual marching season starts around April/May and can last until the end of September. This is a time when those children and young people with Type 1 Diabetes Mellitus who are involved in parades, need advice from the diabetes team regarding the variations in their activity levels. This can be a very delicate subject within the cultural setting, revealing their allegiance for one side of the community or the other and can be very sensitive. As a result, patients or parents may ask veiled questions about these events but seek clear guidance about 'long walks whilst carrying a drum' to avoid swings in their blood glucose levels, allowing them to participate. The team must read between the lines and delve deeper in a sensitive way as the 'long walks' can be continuous or sporadic in nature and each patient may be participating for a different reason. This leads us to an explorative discussion about the effect of anaerobic and aerobic exercise on their blood glucose levels and how to manage this, especially using a basal bolus regimen. The recommendations need to be individually based, and often leave little time for testing the advice out before the event. In the midst of this vague discussion, variations in the weather, interpretation of the 'long walk' and change in diet can lead to a tricky conundrum. These enquiries need the advice of the whole multidisciplinary team. Often the family will 'open up' better to the nurses, especially if they feel the nurse has realised the reason for the 'long walk'. The dietitian is invaluable in offering dietary advice for the different types of activity and the prescribers within the team advise on adjustment to the regimen pre, during and post the activity. We discuss one such case & the advice provided.

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Miscellaneous 2

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An evaluation of the experiences with services in wales for children and young people and their families with prader willi syndrome (PWS)

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Introduction
Prader Willi syndrome (PWS) is a complex neurodevelopmental genetic condition which is characterised by hyperphagia, endocrine dysfunction, behavioural and psychiatric issues. Current literature recommends a multi-disciplinary approach to PWS management to tackle its multi-faceted manifestations. No previous study has examined the views and satisfaction levels relating to the services provided for children with PWS in Wales.
Methods
Semi-structured interviews were conducted with participants ($n = 18$) with a mean age of children discussed was 7.6 years. The study included a patient satisfaction survey which were audio recorded, transcribed, and then analysed using thematic analysis.
Results
The results of this evaluation demonstrated behaviour and dietary concerns to be the areas participants find the most challenging about management of PWS. Current overall satisfaction scores amongst participants in the study was 6.41/10 with dietary services particularly regarded as lacking in specialist dietician input. 53% of participants were "somewhat satisfied" with the services they were receiving currently. Common themes in the study included a lack of information given at the time of diagnosis and the need for the service to include specialist understanding of the condition. Services were felt to be accessible to families however there was a need for participants to be proactive in their search for support and there were some issues regarding communication and integration of services across different areas of Wales. Emotional and psychological support was commonly referred to as lacking in the services in Wales.
Conclusions
An overarching theme evaluation was the need for the services provided to be tailored towards PWS. The evaluation has highlighted a need for greater awareness and psychosocial support for not only the children with PWS in Wales but the parent and carers receiving the diagnosis and managing the condition. It is recommended that the patient pathway that has been drafted here should be presented amongst health professionals and to establish a PWS support group in Wales overseen by healthcare professionals to ensure that a sense of fear for the future is not created. The evaluation demonstrates the importance of evaluating patient satisfaction with services as a method to make improvements to quality of care.

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Osteoma cutis and medulloblastoma due to heterozygous inactivating GNAS mutation – a rare association due to reduced GNAS expression in tissues

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Introduction
Primary Osteoma Cutis is associated with Albrights Hereditary osteodystrophy (AHO) due to inactivating *GNAS* mutation. It is inherited in an autosomal dominant or sporadic manner. Phenotype in *GNAS* mutation is varied due to parent specific gene expression. Maternally inherited *GNAS* mutation leads to hormone resistance, but paternally inherited mutation leads to AHO features without hormone resistance. Medulloblastoma is the most common malignant brain tumour in childhood. There is a rare association with germline mutations in *GNAS* causing medulloblastoma. We report a case with this rare combination.
Case History
A 2-year-old boy presented with multiple small discrete plaque like lesions in the skin his trunk and limbs. He was born at 37 weeks without any antenatal or postnatal complication except for neonatal jaundice. He was noted to have fleshy plaque like lesions under the skin over his abdomen during the neonatal period which spread to other areas over time. Skin biopsy of the lesion revealed osteoma cutis which prompted the genetic testing. He was diagnosed with heterozygous mutation in *GNAS*. His biochemical investigation didn't reveal any hormone resistance. He had mild developmental delay. He also had a non-traumatic right fibula fracture at 1.5 years which healed subsequently and seems unrelated to his underlying condition. He had a normal Bone health index (BHI) of 3.9 (+0.8 SDS). He presented at the age of 2.5 years with unsteady gait, lethargy, divergent squint and vomiting with cerebellar signs. MRI brain revealed a posterior fossa tumour without evidence of metastatic spread. He underwent complete surgical resection. Histology revealed desmoplastic nodular medulloblastoma, SHH molecular group. He received chemotherapy according to the HIT-SKK protocol. Tumour next generation sequencing was normal, including MYCN, MYC, CTNNB1 and TP53. Whole genome sequencing of the tumour confirmed *GNAS* mutation.
Discussion
Somatic *GNAS* mutation has been identified in several tumours including medulloblastoma. Germline inactivating *GNAS* mutation have been rarely identified in SHH activated medulloblastoma group in the recent years. Reduced expression in *GNAS* in tumour tissues lead to poorer prognosis. This case highlights the importance of vigilantly looking for medulloblastoma when children with underlying germline *GNAS* mutation present with neurological symptoms.

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Evaluation of a new multidisciplinary clinic for the endocrine assessment of patients with duchenne muscular dystrophy

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Introduction
The endocrine assessment of children with Duchenne muscular dystrophy (DMD) can be necessary for management of osteoporosis, delayed puberty, obesity, adrenal insufficiency, and short stature. With ongoing implementation of the international standards of care for DMD, referrals to our Metabolic Bone Clinic (MBC) increased beyond its capacity, impacting patient care. The neuromuscular and endocrine departments implemented a new referral pathway and Multi-disciplinary Clinic (MDT) to address patients' needs more effectively. The MDT runs every other month for one hour. We aimed to evaluate this new clinic by: (1) whether patients were assessed according to the new referral pathway; (2) the time from referral to clinic assessment; and (3) the effect on the Metabolic Bone Clinic capacity.
Methods
We identified children with DMD that attended the MDT and the MBC from September 2021 to March 2022. Data collected included: referral date, referral

criteria, auxology, treatment and follow-up plan. Data were extracted prospectively from the electronic patient record.
Results
In total, 40 patients were seen in four MDTs over six months: median 10 patients/clinic. New referrals totaled 40/45 (88%). The reason for referral aligned with the new pathway in 33/40 (82%); most frequently for bone mineral density deterioration (23/40; 57%) and asymptomatic vertebral fracture (11/40; 27%). 'Other' was the only reason for referral for 13/40 (17%). MDT review was scheduled within a median of 6 weeks (range 0-15) from referral; and 28/40 (70%) were seen at the next scheduled clinic. New treatment was started in 13/45 (28%) patients, most frequently Bisphosphonates (11/45; 24%). Of new referrals, 7/40 (16%) were referred to MBC; remainder were discharged to the Neuromuscular Clinic (12/40; 27%) or followed up in the MDT (21/40; 47%). In total, 15 patients were seen in 12 MBCs over the same period, including two new referrals. Follow-up was requested for 6/15 (40%) and the remainder were discharged (to MDT, Neuromuscular Clinic, or adult services).
Conclusion
A new Multidisciplinary Clinic between Neuromuscular and Endocrine teams successfully followed a new referral pathway for the endocrine assessment of children with DMD; assessed patients within an acceptable timeframe; and increased Metabolic Bone Clinic capacity.

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Evaluation of an educational intervention on puberty/pubertal induction in adolescent girls with turner syndrome

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In 2019, we attended a patient engagement zoom session, hosted by Turner Syndrome Support Society (TSSS), to launch a video illustrating the use of a transdermal patch for pubertal induction in girls with Turner Syndrome (TS). Several girls raised to us that they felt that they did not have a good understanding of puberty, and on why it was important to receive both oestrogen and progesterone preparations during pubertal induction. To target this, we developed an explanatory video for young people and their families to explain the role of the main hormones in puberty and the menstrual cycle, and the importance of both oestrogen and progesterone in TS hormone replacement therapy (HRT). This video was released onto the TSSS YouTube Channel, available free of charge to patients and their families.
Objective
To assess the effectiveness of a video educational intervention to increase understanding of puberty and HRT in girls with TS.
Methods
Approximately 15 attendees joined us for a patient and family evening hosted by TSSS to discuss and promote the video. All girls who had attended were emailed, with prior consent, with a short questionnaire. Before and after watching the video girls were asked to rate their understanding of the following on a likert scale: puberty; the menstrual cycle; the use of oestrogen in pubertal induction; the use of progesterone in pubertal induction (1 = no; 2 = some; 3 = good; 4 = excellent). Responses were anonymised.
Results
Five girls responded. Four girls (80%) reported an improvement in understanding across all of the topics covered. No respondent felt they had an 'excellent' understanding of the topics before the video, with only 1 respondent feeling they had a 'good understanding'. All respondents felt they had at least a 'good understanding' in all topics after watching the video.
Conclusion
Most girls reported only 'some understanding' of puberty, the menstrual cycle, and the use of oestrogen and progesterone prior to watching the video, which improved following watching the video. Short educational videos are an effective way of increasing understanding of key health topics in girls with TS.

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Central precocious puberty in a patient with short stature and skeletal abnormalities in KBG syndrome due to ANKRD11 variant

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Introduction
Underlying causes of short stature are difficult to establish and many patients with short stature do not have a clear diagnosis. Careful examination and investigation of patients with short stature may identify additional features that help to make a diagnosis or direct genetic testing. Here we describe a patient with severe short stature with additional features on examination and skeletal survey in keeping with KBG syndrome. In addition, the patient developed CPP which is a rarely reported feature of KBG syndrome. KBG syndrome is most frequently caused by mutations in *ANKRD11*. The most significant features include developmental delay, skeletal abnormalities (typically costovertebral abnormalities) and abnormal facies (macrodontia, craniofacial abnormalities and low hairline). We present a patient with a rare mutation in *ANKRD11* with typical skeletal abnormalities and central precocious puberty (CPP).
Case presentation
A 5-year-old girl was referred for short stature with a background of autism, severe learning disability, sleep disturbance, bilateral hearing loss, constipation and abnormal hand movements. Birth weight was 3.2 kg. Height was 96.9 cm (-2.2 SDS), weight 14.8 kg (+0.2 SDS), BMI 15.8. Additional features included bilateral clinodactyly, foetal finger pads, broad toes, low hair line, mid facial hypoplasia, short neck, simple ears and macrodontia. Skeletal survey revealed wormian bones, bilateral cervical ribs, and macrodontia. Bone age was delayed by 2.5 yrs. Genetic testing revealed a previously described *ANKRND11* variant c.1903_1907del; p.(Lys635Glyfs*26). She then developed into puberty before age 8 years. LHRH test at 8.7 years showed a LH peak 6.3 IU/l, FSH peak 9.3 IU/l, in line with CPP. She commenced on GnRH-analogues.
Conclusion and learning points
ANKRND11 is a chromatin modulator affecting growth by increasing P21, a cell cycle inhibitor. The role of ANKRD11 in pubertal development is unknown. This case highlights features that direct clinicians towards a diagnosis of KBG syndrome, including macrodontia, costovertebral abnormalities. CPP has been described rarely in patients with KBG syndrome but can be added to features that may help to direct to a diagnosis of KBG syndrome. Other syndromes with short stature and early puberty include Temple syndrome and Williams Syndrome.

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Management challenges in a patient with APECED due to endocrine and nonendocrine multisystem involvement

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Introduction
Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) is an autosomal recessive condition due to mutation in the autoimmune regulator (AIRE) gene which leads to a variable phenotype with endocrine and nonendocrine multisystem involvement. We present a challenging case of APECED with auto immune hepatitis, mineralocorticoid deficiency and short stature.
Case history
A 8-year-old girl born to consanguineous parents, presented at five months of age with oral candidiasis. At the age of one year, she developed persistent diarrhoea, skin, and nail infection. Aged four years, she presented with hypocalcaemic seizures and was diagnosed with hypoparathyroidism. She was started on alfacalcidol and calcium supplementation. At the age of 6 years, she was noted to have elevated liver enzymes with positive LKM antibodies. Liver biopsy revealed chronic hepatitis, for which she was started on prednisolone. She had a normal cortisol response to synacthen prior to starting prednisolone. The adrenal, thyroid peroxidase, GAD65, pituitary and intrinsic factor antibodies were negative. She was diagnosed with homozygous AIRE c.278T > p.(Ley93Gln) variant inherited from both parents. Her elder sibling had died at the age of 1 year due to suspected liver disease. At the age of 7.5 years, she presented with persistent hyponatremia and the renin was high with normal aldosterone level. The repeat adrenal antibodies were positive, and she was started on fludrocortisone and salt supplementation. She was on itraconazole for her onychomycosis nail infection and continued prednisolone for the hepatitis. It is likely that the prednisolone masked the onset of autoimmune adrenal insufficiency. Her growth was noted to be faltering despite normal dietary intake. IGF1, IGFBP3 and growth hormone stimulation test were normal. The renal function, ESR, fecal calprotectin and pancreatic elastase 1 were normal.
Discussion
APECED is a monogenic condition with immune dysregulation leading to multisystem autoimmune disorders predominantly affecting endocrine system. Depending on the genetic mutation varying degree of gastrointestinal manifestation has been reported in the literature presenting with growth impairment. Autoimmune enteropathy due to loss of enteroendocrine cells is a rarely identified entity.

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Three different presentations of a rare monogenetic cause of hypoparathyroidism in a small district general hospital

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Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dystrophy (APECED), is a rare autosomal recessive cause of polyendocrinopathy. Mutations in the AIRE (Autoimmune regulator) gene results in failure of T cell tolerance. APECED occurs in about 1 in 90,000 to 1 in 200,000 people but is more prevalent in certain groups (Iranian Jews, Sardinians, and Finns). Its presentation depends on the gene mutation. The classic triad of symptoms are chronic mucocutaneous candidiasis, hypoparathyroidism and adrenal insufficiency, though many other autoimmune disorders can also occur. The following cases represent a snapshot of the diversity of presentations in this condition. Case 1: A 3-year-old boy of consanguineous parents presented following an afebrile seizure, which resolved without intervention. However, there was a background of weight loss, recurrent oral thrush and other recurrent infections needing multiple courses of antibiotics. Clinical examination was normal but his bloods demonstrated a severe hypocalcaemia (adjusted calcium 1.05 mmol/l). He improved with treatment and was subsequently diagnosed with APECED. His condition unfortunately progressed and he developed adrenal insufficiency aged 5 years. He had a further presentation with symptomatic hypercalcaemia but has remained well since. Case 2: A 2-year-old girl was referred to ED with incidental finding of hypocalcaemia (adjusted calcium 1.66 mmol/l). However, there was a background of thrush, constipation and a family history of APECED. Her parents are consanguineous. She improved with treatment and was subsequently discharged home. Unfortunately she re-presented with an afebrile seizure, likely secondary to rapid decrease in dose of calcium supplements (as her calcium levels, though low, remained stable), once corrected, the patient was discharged home. Case 3: A 2-year-old girl presented with three days' of abnormal gait, morning leg stiffness and not weight-bearing. There was no concurrent illness. Apart from a background of constipation, she was normally fit and well. On examination, she had clear signs of tetany. Bloods confirmed hypocalcaemia (adjusted calcium 1.45 mmol/l), hypoparathyroidism and vitamin D deficiency. Her symptoms improved and she was subsequently discharged. However she re-presented with ongoing symptoms of Covid-19 pneumonitis resulting in admission to a respiratory tertiary centre. This prompted further investigations and she was subsequently diagnosed with APECED.

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Obesity 2

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Semaglutide as a safe and effective weight loss treatment in children with obesity

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Background
A quarter of UK children now leave primary school obese. Childhood obesity is associated with significant comorbidity including obstructive sleep apnoea, type 2 diabetes, non-alcoholic fatty liver disease, hypertension and depression. We report our experience of using semaglutide, a weekly subcutaneous GLP1 receptor agonist, as a weight-loss adjunct for severely obese children in combination with dietary and lifestyle support from a multidisciplinary team.
Method
Data from all children in our tertiary weight management service treated with semaglutide 1 mg were reviewed retrospectively. Demographic data including age, gender, medical diagnoses and comorbidities associated with obesity were collected. Primary outcomes were changes in weight, BMI, BMI standard deviation score (SDS) and percentage excess weight after 6 months of treatment. Secondary outcomes were side effects and tolerability.
Results
18 patients (9 male) between 10 and 17 years old were prescribed semaglutide. All except one had a BMI SDS >3 with at least one weight-related complication. Two patients had a confirmed genetic cause for obesity and 7 had autism. Treatment with semaglutide for 6 months produced a mean BMI SDS decrease of 0.27 and a mean weight loss of 6.1 kg (mean reduction in excess weight of 16%). Four patients completed 12 months of treatment with a mean BMI SDS reduction of 0.74. This compares to a mean BMI SDS reduction of 0.4 over 2 years in our weight management program without a GLP1 receptor agonist. Five patients reported side effects (gastrointestinal upset, fatigue and hair loss). One patient discontinued treatment due to side effects.
Discussion
Our experience shows that semaglutide is a safe and highly effective weight loss adjunct in children with co-morbid obesity, although it is not yet licensed in this age group. Currently the only GLP1 receptor agonist licensed for children with obesity is liraglutide. However, adult data demonstrated that semaglutide is better tolerated and more effective at a high dose of 2.4 mg weekly compared to liraglutide for weight. Semaglutide is also given as a weekly rather than daily injection. Further long-term studies examining whether the effect plateaus and potential rebound weight gain after stopping are needed.

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Incidence and predictors of the complications of childhood obesity

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Introduction
Paediatric obesity is associated with significant long-term complications. This study investigated features of metabolic syndrome, non-alcoholic fatty liver disease (NAFLD) and obstructive sleep apnoea (OSA) aiming to establish their incidence and identify any predictive factors.
Methods
A retrospective review of case notes was performed for children aged 2-16 years managed for investigation and management of obesity within a single tertiary endocrine centre over 2 years.
Results
101 children were included (median age at presentation 11.3 years, 49% male, mean body mass index (BMI) standard deviation score (SDS) at presentation 3.5). The following prevalence of comorbidities were noted - biochemical insulin resistance (IR) 60%, impaired glucose tolerance (IGT) 12%, type 2 diabetes mellitus (T2DM) 5%, NAFLD 19% and OSA in 12%. Increasing age correlated with fasting insulin ($r=0.42$, $P<0.001$), fasting glucose ($r=0.25$, $P=0.01$) and HbA1c ($r=0.25$, $P=0.03$); and was predictive of IGT (mean difference 1.9 years, $P=0.02$). Sex and pubertal status did not affect the incidence of complications arising. BMI SDS was not predictive of complications arising, except for OSA (mean difference 0.5 SDS, $P=0.03$). A correlation was noted between IR and NAFLD ($P=0.02$). The positive predictive value (PPV) for acanthosis nigricans (AN) predicting IR was 88% and the negative predictive value (NPV) was 42%. This was similar between the two major ethnic groups studied – Caucasians (PPV 91%, NPV 47%) and south-east Asians (PPV 88%, NPV 40%).
Conclusion
The complications of obesity are relatively common – supporting the need for the recently nationally commissioned Complications of Excess Weight clinics, to help reduce and prevent long-term co-morbidities. Increased age is an important predictor of metabolic syndrome. Therefore, a greater focus on prevention and management strategies is needed at a younger age. AN is a recognised clinical marker of IR, however this study demonstrates that the absence of AN cannot reliably exclude IR. This suggests the need for biochemical testing for IR, even in the absence of AN, in the context of obesity where its prevalence is so high.

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P78

Evaluating glycaemic variations in children and young people with obesity using continuous glucose monitoring

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Introduction
Type 2 diabetes mellitus is a known complication of childhood obesity. It is currently diagnosed by undertaking an oral glucose tolerance test (OGTT). Continuous glucose monitoring (CGM) is used predominantly by patients with type 1 diabetes mellitus to monitor glucose levels.

Aim
The aim of the study was to investigate glycaemic variation in children and adolescents with obesity who have had no evidence of pre-diabetes or type 2 diabetes on OGTT, with the use of CGM.
Methods
Children and young people (aged 2-18 years) with obesity (BMI SDS >2) who have had a recent normal OGTT were recruited. Free-living blinded CGM was commenced for a minimum of three days using Dexcom G6 devices, which were successfully inserted into the back of the upper arm.
Results
In total, 13 patients were studied with a mean age of 14.4 years (range: 10.3-16.6). The average BMI was 40.2 kg/m^2 ($+$ 7.3 SD) and mean BMI SDS was $+3.5$ ($+$ 0.5 SD). The average HbA1c was 34 mmol/mol (5.3%). The CGM devices were worn for an average of 8.0 days (range: 3.4-11.9). The mean glucose of all patients was 6.3 mmol/l ($+$ 1.2 SD) and the average coefficient of variation was 19.8% (range: 14.3-45.9; normal $<36\%$). Percentage time in and out of range showed a median time between 3.9 and 7.8 mmol/l (70-140 mg/dl) of 83.5% (IQR 79.9-93.7). The median time with glucose levels over 7.8 mmol/l (140 mg/dl) was 12.5% (IQR 2.5-16.7) and median time spent with glucose levels over 10.0 mmol/l (180 mg/dl) was 0.1% (IQR 0-1.6).
Conclusions
The results show that the median time spent in target glucose range was 83.5%, which is lower than the expected 95% seen in healthy, non-diabetic participants. We also found that the patients' glucose levels were rising above 10 mmol/l (180 mg/dl) occasionally. Glycaemic dysregulation has been identified in our paediatric population with obesity, where conventional investigations were noted to be normal. This shows the potential role for CGM in recognising glycaemic variations earlier, which would help with implementing appropriate treatment strategies.

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P79

Baseline health-related quality of life in UK children and adolescents with severe obesity

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Introduction
Childhood obesity is associated with several complications related to physical and mental health. Determining health-related quality of life (HRQOL) is an important outcome measure to ensure patients receive the appropriate care.
Aim
We report the baseline HRQOL in a group of UK children and adolescents with severe obesity who were managed in a Tier 3 weight management service.
Methods
Paediatric quality of life (PedsQL) 4.0 Generic Core Scales questionnaire, a validated tool was used.
Results
53 patients completed the PedsQL measure at baseline (at the time of their first assessment by the Tier 3 service). The average age was 13.3 years (range: 6-17) with 50.9% (27/53) of the cohort being female. The median body mass index (BMI) was 40.6 kg/m^2 (IQR 35.1-46.0). Table 1 shows the results for the child self-reported tool. The transformed scores are out of 100, with the highest score indicating better HRQOL. The results showed a median total score of 57/100 (IQR 45.3-64.8). The patients scored lower in psychosocial health, compared to physical health. All results are lower than those previously published in healthy individuals (mean range across scores 79.2 to 87.8). The linear regression analysis with BMI as the independent variable showed no significant association between BMI and the individual scales probably because all BMI measures were at the higher range.
Discussion
The results have shown that HRQOL in children and young people with significant obesity is low with the total score being only 57/100. Psychosocial health is impacted more than physical health. This baseline data will help provide targeted support for improving mental health in this cohort and can also be used to monitor the response to the input from the MDT weight management service.

Table 1 shows the results of the child self-reported PedsQL questionnaire in our cohort of patients

Scale	Median (IQR) of Transformed Score (0-100)
Total Score	57.0 (45.3-64.8)
Psychosocial Health Summary Score	55.0 (41.7-63.3)
Physical Health Summary Score	62.5 (53.6-71.9)
Physical Functioning	62.5 (53.6-71.9)
Emotional Functioning	50.0 (35.0-60.0)
Social Functioning	60.0 (50.0-75.0)
School Functioning	50.0 (35.0-60.0)

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P80

The use of GLP-1 agonist in an adolescent with type 1 diabetes mellitus and obesity

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Introduction
Childhood obesity continues to prove a major public health concern, with obesity and metabolic syndrome becoming increasingly prevalent in children and young people with type 1 diabetes mellitus (T1DM). Glucagon-like peptide 1 (GLP-1) therapy has shown promising results for weight loss in adults with type 2 diabetes mellitus (T2DM) and has recently been licensed for the treatment of adolescents living with obesity. Liraglutide has been shown to be beneficial in few adult studies by improving glycaemic control and promoting weight loss in patients with T1DM as an adjunct to insulin therapy. There is no such data available for children or adolescents with T1DM. We report the use of Liraglutide in an adolescent with T1DM and significant obesity.
Case Report
A 16-year-old female with T1DM, coeliac disease, fatty liver, and dyslipidaemia was noted to be gaining weight rapidly after the diagnosis of T1DM at the age of 14 years. She was managed with insulin therapy and continuous glucose monitoring (CGM). Weight upon diagnosis was 76.6 kg ($+2.31$SDS). Since diagnosis, the weight continued to escalate rapidly [40.4 kg weight gain in a 12-month period]. Challenges in diet management, altered sleep pattern and lack of physical activity contributed to the weight gain. Despite attempts at lifestyle modification and intense input from MDT, the weight rose to 122.8 kg ($+6.83$ SDS) with a BMI of 43.8 kg/m^2 ($+3.70$ SDS). Hence, Liraglutide was commenced at a dose of 0.6 mg once daily and increased to a maximum dose of 3 mg over a 6-week period with close monitoring of blood glucose. Following this, the weight escalation slowed down and the latest BMI has dropped slightly to 43.0 kg/m^2 ($+3.64$ SDS). No change in glycaemic control has been noted and there were no side effects.
Conclusion
GLP-1 therapy has the potential to support weight loss in adolescent patients with T1DM and obesity. However, long term data is necessary to assess the safety and efficacy. Further studies would help to establish the long-term benefits of GLP1 analogues (in terms of glycaemic control and weight loss) in adolescents with T1DM.

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Pituitary and Growth 2

P81

A novel IGF1R variant in a child with mild IGF1 resistance, normal birth weight, mild short stature and microcephaly

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Introduction
The insulin-like growth factor 1 receptor (IGF1R) gene, located on chromosome 15q26.3, encodes the 1367 aa tyrosine kinase receptor IGF1R which is involved in many processes, including growth. Few heterozygous mutations of IGF1R leading to IGF-I resistance have been described in patients with intrauterine and postnatal growth retardation, microcephaly and variable learning difficulties. We report previously undescribed IGF1R nonsense variant in a child with normal birth weight, mild short stature, and microcephaly.
Case
A 9-year-old male presented at 5.4 years with mild short stature (Height -2.1 SDS) low BMI (-2.6 SD) and microcephaly (Head circumference -3.9 SDS). His height velocity was 6–7 cm/year increasing his height to -1.75 SD. Birth weight was normal (1.38 kg at $31+6$ weeks (-1.25 SDS). He also has a squint, delayed developmental milestones, behavioural difficulties and requires learning support. There was no significant family history. Maternal height was -1.39 SDS; paternal height -0.89 SDS.

Results
IGF1 was consistently mildly raised [aged 5.4 years, 228 mg/l (15.6-216.4), aged 6.6 years, 338 mg/l (18-307)] with IGFBP-3 at the upper normal range [4.1 and 5.4 mg/l (1.9-5.2)], raised random GH concentration (8.7 mg/l), in line with IGF1 resistance. Bone age was normal. Spine X ray showed mild scoliosis and brain MRI reduced white matter. Sanger sequencing of IGF1R showed a nonsense variant (c.1237C>T, p.Gln413*), generating a premature stop codon. This variant has not been reported in control databases (dbSNP, 1000 Genomes, ExAC and gnomAD, Human Gene Mutation Database, ClinVar and LOVD) and has been classified as pathogenic using ACMG criteria and bioinformatic predictors (SIFT, PolyPhen-2, Mutation Taster). The mother did not carry the IGF1R variant.
Discussion
In conclusion, the novel heterozygous nonsense IGF1R variant c.1237C>T (p.Gln413*) results in mild impairment of IGF1R signalling with mild GH and IGF1 overproduction, and a phenotype of mild short stature without SGA but with significant microcephaly. Our patient fulfils 3 of the 4 previously proposed criteria for IGF1 resistance. This result suggests that IGF1R should be investigated in patients with biochemical evidence of IGF1 resistance even in the absence of short stature or SGA.

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P82

Glucagon tolerance tests in a tertiary paediatric centre: an evidence-base for protocol refinement

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Background
The glucagon tolerance test (GTT) is used to diagnose growth hormone deficiency (GHD) in younger children or in patients where the insulin tolerance test is contraindicated. We assessed GTTs carried out over five years in a tertiary paediatric centre to assess growth hormone (GH) and cortisol axes. The aim was to assess at which time points the GH peak was observed, and assess whether any predictive value is gained from demographics or IGF-1.
Methods
55/58 tests (3 excluded due to incomplete data) from 52 patients were analysed. We assigned risk groups based on indication; high-risk referring to oncology patients (3/55) and low risk to patients with isolated short stature and syndromic patients. Z-scores were used for height, weight, BMI and IGF-1 concentration (sex, age adjusted). A binary logistic regression was performed to analyse height, weight, BMI and IGF-1 Z-scores for both normal and abnormal GH results.
Results and Discussion
In 19/55 (35%) tests the GH response was suboptimal (<6.7 mg/l). The peak sample precluding GHD occurred at 120 minutes from glucagon administration. No diagnostic samples occurred before 60 and after 180 minutes. Cortisol response was suboptimal (<420 nmol/l) in 10/55 tests. The lowest glucose levels were recorded at 90 (26/55 tests) and 120 (21/55 tests) minutes. Hypoglycaemia (<2.2 mmol/l) occurred in 9/55 (16%) tests. All three high-risk patients had GHD. Patients with GHD had significantly lower IGF-1 (mean Z-score = -1.21 for GHD, -0.61 for non-GHD, $P=0.009$). No significant difference was found when comparing height, weight and BMI Z-scores between GHD and non-GHD groups.
Conclusion
The mode single peak sample precluding GHD occurred at 120 minutes from glucagon administration followed by the 90 minute time point. IGF-1 was lower in the GHD group. We suggest adding a time-point at 105 minutes to reduce the false positive rate. We also note that a spontaneous peak prior to glucagon administration doesn't preclude a second peak later during the test.

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P83

DNA haplotypes influencing the response to growth hormone therapy are disproportionately inherited from neanderthals

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Background
Neanderthals split from an ancestral human population ~500,000 years ago and lived in Eurasia until 40,000 years ago. Early modern humans emerged in Africa ~350,000 years ago migrating into Eurasia 50,000 years ago. Interbreeding occurred between early modern humans and Neanderthals leading to the introduction of Neanderthal DNA into the early human population, a process termed introgression. In modern Eurasian populations around 2-4% of DNA is of Neanderthal origin. The aim of this study was to examine whether genomic factors linked to response to growth hormone (GH) therapy are enriched for elements inherited from Neanderthals and whether these had been subject to selection during subsequent human evolution (a process referred to as selective sweep).
Methods
We identified 11 genes where transcript levels related to first year growth hormone response[1] and 17 SNPs related to growth hormone response from the PREDICT study[2] and a recent genome wide study[3]. These were mapped to known regions inherited from Neanderthals[4]. For each genomic region we calculated the minimum Neanderthal sweep score, normalised for genomic region length and compared this to sweep score in 10,000 randomly selected gene regions.
Results
7 of the 11 transcripts and 13 of the 17 SNPs were located in regions with haplotypes inherited from Neanderthals providing strong evidence of Neanderthal introgression. Of the 17 SNPs, five had been included in the Neanderthal selective sweep scan[4] and two of these 5 SNPs were identified as introgressed alleles. Median and Minimum Neanderthal selective sweep score across the year one growth response genes were negative but significantly lower than the randomly selected genes ($P=4.88e^{-13}$) indicating positive selection over time.
Conclusion
The genetic response to recombinant human growth hormone is enriched for regions showing evidence of introgression from Neanderthals with sweep scores indicating positive selection of these regions over time. Utilising Neanderthal haplotype data may optimise development of genetic tests predicting growth hormone response.
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P84

Panyiatopoulous syndrome in the setting of precocious puberty

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We present the case of a girl with rapidly progressing central precocious puberty, CPP. The young girl presented with consonant rapidly progressive puberty and onset of menarche. She had onset of breast budding at 7 years 11months, menarche at 8 years 2 months, with significant growth spurt. Periods continued every 3 weeks. A Brain MRI demonstrated a dysplastic lesion of her tectal plate. She underwent treatment with Gonadotropin releasing hormone analogues to suppress puberty. The girl went on to develop strange episodes at night when puberty was not suppressed. A EEG demonstrated features consistent with Paniyatopoulous syndrome. After commencing gonadotropin releasing hormone analogues, the strange episodes resolved. However they reoccurred prior to her next injection, associated with elevated LH. When injection frequency was increased, seizures resolved. Puberty is well known to be both a trigger for pre-existing epilepsy syndromes and a time when new seizures can emerge, presumably due to hormonal influences on neurobiology. With this case we encourage the clinician to be vigilant for seizures in patients with precocious puberty.

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P85

Abstract Withdrawn

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Thyroid

P86

Congenital hypothyroidism: should radioisotope scanning be made mandatory to improve etiological diagnosis?

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Aim
To evaluate current practices relating to diagnosis and treatment of congenital hypothyroidism (CHT) in Aneurin Bevan University Health Board (ABUHB) compared to national guidelines and the use of radioisotope scanning in improving etiological diagnosis.
Method
This service evaluation used a database of paediatric hypothyroid patients in ABUHB. Only children with CHT were included and any children born before January 2014 were excluded. 30 children met these criteria. Clinical notes from Clinical Workstation (CWS) were evaluated on the 30 children. This included how a diagnosis of CHT was made, time from referral to paediatric review, repeat TFTs for the infant, TFTs for the mother, time from diagnosis to commencement of treatment with levothyroxine and whether ultrasound scanning (USS) or radioisotope scanning of the thyroid was performed.
Results
All infants met guidelines for receiving newborn blood spot screening (NBS), further testing and paediatric review following referral. 94.44% of mothers had evidence of TFTs. 94.44% of infants were started on levothyroxine within an appropriate timeframe. All infants received an USS of thyroid and results demonstrated 19 eutopic thyroids, 4 ectopic, 6 absent and 1 unknown. 23 (76.67%) infants had a radioisotope scan performed which showed 10 thyroids with normal uptake, 8 ectopic, 2 agenesis, 1 dysplasia and 1 other. Radioisotope scan detected 4 ectopic thyroids that were missed following USS alone.
Conclusion
Radioisotope scanning was found to be better at detecting ectopic thyroid tissue than USS. Therefore, it is recommended that radioisotope scanning is performed in a greater number of children with CHT to improve the accuracy of etiological diagnosis and to ensure ectopic thyroid tissue is not missed.

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P87

Congenital hypothyroidism due to PAX8 gene mutation – a case report

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Introduction
Congenital hypothyroidism (CH) occurs 1 in 3,000-4,000 live-births. The causes of CH can be divided into two groups: thyroid developmental defects (thyroid dysgenesis) and inborn errors of thyroid hormone biosynthesis (dyshormonogenesis). Although mutations in paired box gene 8 (PAX8) usually cause thyroid dysgenesis, they have been reported in association with eutopic thyroid gland without function. PAX8 has been described to have a role in regulating the expression of sodium/iodine symporter in humans. We describe a rare case of CH with eutopic thyroid gland due to a heterozygous PAX8 mutation.
Case report
The proband was born at term by normal vaginal delivery to non-consanguineous parents. Her birth weight was 3390grams. Mother had gestational diabetes and antenatal (26 weeks) scan showed polyhydramnios. There was no family history of thyroid disease. She presented on day 5 of life with reduced feeding and excessive weight loss. On examination she had low muscle tone and soft distinctive facial features which prompted the paediatric team to perform thyroid function tests (TFTs). The result showed normal free thyroxine (fT4) - 21.8 pmol/l (normal 11.0-21.2) and elevated Thyroid Stimulating Hormone (TSH) - 29.5 mIU/l (normal 0.27- 4.2). Persistently elevated TSH (19.6 mIU/l) with normal fT4 (19.2 pmol/l) on repeat bloods a week later, triggered Technetium thyroid uptake scan. No uptake of Technetium in the neck region, suggestive of thyroid aplasia. Normal serum free T4 and detectable serum thyroglobulin (128 mg/l) was inconsistent with thyroid aplasia. Subsequent neck ultrasound confirmed a normal shape, size, position and morphology of thyroid gland. Suspecting iodine transport defect due to discrepancy in Technetium scan and thyroid ultrasound results, genetic testing was performed. Targeted next generation sequencing identified a pathogenic heterozygous mutation in PAX8 (c.619C > T, p.Arg207*). Genetic testing for parents is in progress to determine if the variant has arisen *de novo*. Levothyroxine (25 mg) was commenced at two weeks of age and follow up TFTs have been normal.
Conclusion
Although detection rate of pathogenic mutations in thyroid dysgenesis is low, it is important to consider genetic analysis of atypical presentations as increased mutation detection rate is likely. Identification of genetic mutations help in screening for conditions associated with CH.

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P88

Hypothyroidism - unknown through the known

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Hypothyroidism is a well-known cause of delayed puberty in children. But in rare instances, hypothyroidism can also be related to isolated menarche. The mechanism remains debatable whilst the overall incidence of the condition remains unknown.
Case Report
6-year girl presented to children's emergency with 2 days history of vaginal bleeding. Mum reported her being intolerant to cold, constipated and faltering growth compared to her twin sister. Her skin was cold and clammy and she had a hoarse voice but no breast budding, secondary sexual characters, or goiter. Her weight was on the 25th centile and height between 0.4th and 9th centile. All observations were normal including blood pressure. Investigations confirmed severe primary hypothyroidism [very low Free T4 2.1 pmol/l, with very high thyroid-stimulating hormone (TSH) > 100mU/l) and raised Thyroid peroxidase antibody (TPO). Her anterior pituitary functions showed raised prolactin 1840 mg/l, mildly raised follicle-stimulating hormone (FSH) 4.6 IU/ml and normal luteinizing hormones, estradiol and Cortisol. Pelvic ultrasound showed a left ovary containing follicles with a pre-pubertal uterus. Treatment was started with 50 mg of Levothyroxine once daily. A month later her symptoms improved and her thyroid function normalized. Although unclear, one of the proposed mechanisms for isolated menarche in profound hypothyroidism is FSH mimicry by a very high TSH (as both TSH and FSH share the alpha subunit) causes follicular stimulation (1). In the absence of negative feedback from thyroid hormone, there is an increased production of TRH which increases the TSH and prolactin in the pituitary gland. Various case reports linking hypothyroidism and precocious puberty have been published with either elevated gonadotrophins along with the development of secondary sexual characteristics or with delayed bone age (2,3). Our child had no signs of central precocious puberty, only mildly elevated FSH, elevated prolactin and isolated menarche. Interestingly, although asymptomatic her twin sister was also diagnosed with profound hypothyroidism a few weeks later. Hypothyroidism should be considered in a girl not only with delayed puberty but also in girls presenting with short stature and isolated early menarche. Delayed bone age and elevated prolactin and/or gonadotrophins could be other indicators for the diagnosis.

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P89

An unusual case of encephalopathy

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We present an unusual case of encephalopathy. Paramedics were called to a 13 year old boy with acute confusion, agitation and incoherent speech. Subsequently he reported he had arm twitching and transient episodes of loss of consciousness for the preceding two weeks with increased thirst and lethargy over the preceding year. He had also progressed rapidly through puberty in the year prior. On presentation his parents denied any infective symptoms or likelihood of substance misuse. On initial assessment he was found to have a fluctuating GCS and due to his level of agitation and combativeness he required intubation for transfer. He was normotensive and normoglycemic. Initial investigations for encephalopathy including a CT brain, lactate and ammonia were normal with no obvious cause identified. He was clinically noted to have a large goitre, left proptosis and a post pubertal status. An EEG confirmed an encephalopathic state but no epileptiform activity was seen. He was extensively investigated for an infective or inflammatory cause of encephalopathy but results were all negative. In view of the goitre TFTS were performed showing a low Thyroxine at 7.9 pmol/l (12.6-21.0 pmol/l) and an elevated TSH of 24.9 mIU/l (0.51-4.3 mIU/l); this widened the differential diagnosis. Anti-Thyroid peroxidase (TPO) antibodies were the performed and found to be significantly elevated at > 600 (Upper limit of normal

25 IU/ml). An US neck showed a swollen, hypervascularised thyroid gland. Early morning Cortisol was satisfactory at 400nmol/l. With the above results a diagnosis of Hashimoto's Encephalopathy/SREAT (Steroid responsive encephalopathy associated with autoimmune thyroiditis) and autoimmune hypothyroidism was made, and he was commenced on IV Methylprednisolone and Levothyroxine. His GCS normalised over the next 48 hours and he was extubated on day 4. He was changed to weaning oral Prednisolone. On review two weeks post discharge he was clinically euthyroid with no palpable goitre, a normal neurological exam and no proptosis. Anti-TPO antibodies had fallen to 414 IU/ml and thyroid function was normalising. This case demonstrates and the importance of a thorough history and clinical examination and it highlights that it is essential to maintain a wide working differential diagnosis.

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P90

2 cases of thyroid hormone resistance

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Thyroid hormone resistance is a rare condition, caused by mutations of the thyroid hormone receptor beta (THRB) gene, inherited in an autosomal dominant manner. This results in decreased tissue sensitivity to thyroid hormone action, the hall mark is high FT4 levels with normal TSH levels. The clinical presentation is variable. We discuss 2 cases of thyroid hormone resistance who received Carbimazole treatment. Case 1 is an 8 year old girl, who was initially misdiagnosed as hyperthyroidism. She was commenced on Carbimazole and Thyroxine 'block and replace' regimen. Anti TPO and anti TSH receptor antibodies were negative. Thyroid ultrasound was normal. Follow up thyroid function testing revealed elevated TSH levels and compliance was queried. Over the following years she developed a large goitre. On review in clinic at the age of 12 years, further questioning revealed a strong family history of thyroid abnormalities. The patient's mother had 'abnormal thyroid tests' which were not treated. Review of her initial results led to a diagnosis of thyroid hormone resistance, which was confirmed on genetic testing. Medication was discontinued and goitre resolved. Case 2, a 12 year old girl was correctly identified as having thyroid hormone resistance. Due to behavioural symptoms she was treated with Carbimazole. Despite dose adjustment, she became clinically hypothyroid with increasing goitre. These cases highlight the importance of correctly diagnosing this rare condition. When considering treating thyroid hormone resistance, it is essential to concentrate on the patient's symptoms and clinical picture instead of aiming to normalize thyroid hormone levels. Most patients overcome the resistance by increased thyroid hormone secretion and do not require treatment. Patients who present with symptoms of hyperthyroidism can be treated symptomatically with beta-blockers or antianxiety medications depending on their predominant symptoms

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P91

A tale of twin thyroids - a report of identical twins with pten hamartoma syndrome, developing different thyroid tumours in early adolescence

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The PTEN gene is a tumour suppressor gene with high risk of breast, thyroid, endometrial, colorectal, kidney tumours and melanoma, mucocutaneous lesions, macular pigmentation, and macrocephaly. Germ line heterozygous pathogenic variants in this gene leads to a spectrum of disease now called PTEN hamartoma tumour syndrome (PHTS). Cowden syndrome (the predominant phenotype of PHTS) is estimated to affect 1:200,000 individuals - however it may be underdiagnosed. Guidelines for screening and management of this disease, published by the UK Cancer Genetic Group in May 2017, advised annual thyroid ultrasound screening from age 16 years. An 11-year-old boy (Case 1) who was previously well with no significant family history, presented with epistaxis and was incidentally noted to have thyroid enlargement. He was found to have multiple thyroid nodules (causing tracheal shift), this together with frontal bossing and moderate hypertrophy of gingivae suggested a diagnosis of Cowden syndrome. This was confirmed with a heterozygous pathogenic variant c.632dupG p(Cys211TrpfsTer32) in the PTEN gene. Case 1 underwent first a hemithyroidectomy aged 12 and then total thyroidectomy, with histology returning follicular carcinoma. Case 1's monochorionic identical twin brother (Case 2) had similar clinical features and he was subsequently found to have the same pathogenic genetic variant. Case 2 underwent total thyroidectomy, aged 13, but on histology, found to have a follicular variant of papillary thyroid carcinoma. Neither child had any evidence of any metastasis. The brothers are both being followed up in a surveillance clinic to undergo further screening for other tumour development risk. Cascade genetic testing confirmed the PTEN pathogenic variant had arisen de novo. Case 1 and 2 are monochorionic identical twins with an identical pathogenic PTEN genetic variant, raised in the same environment. Despite this, they developed different types of thyroid tumours at the age 12 and 13 years. They require ongoing thyroid cancer follow-up according to the MDT recommendations and will continue with PTEN screening into adulthood. These cases suggest that thyroid screening in patients with PTEN hamartoma syndrome would be of benefit earlier than currently advised.

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Multisystem involvement in severe primary hypothyroidism

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A 10-year-old female was referred because of prolonged bleeding lasting for a week following a tooth extraction. She had menarche at the age of 9 years, and since then, she used to have regular heavy periods lasting for over two weeks every month. She had low haemoglobin, prolonged APTT and low von Willebrand antigen level. Therefore, she was diagnosed with von Willebrand disease. At the same time, she was found to have a high TSH and low free T4. She was referred to the paediatric endocrinology clinic because of abnormal thyroid function tests, short stature and possible precocious puberty. Her height was $<$0.4th centile. Tanner staging was B4, A1, and P1. History revealed that she always felt cold, has been constipated for the past 2 years and recently put on weight despite having a low appetite. She also had dry skin and extreme fatigue. There was a family history of heavy bleeding in the mother and older sister but no thyroid problems. Her thyroid functions showed a significantly raised TSH ($>$100 mU/l) and very low free T4 (1.1 pmol/l), positive thyroglobulin and negative anti-TPO antibodies. Baseline gonadotrophins were prepubertal with high FSH. Prolactin was also high. Thyroid ultrasound showed a small thyroid gland with a lobulated outline. Pelvic ultrasound showed a normal left ovary with an enlarged right ovary due to the presence of a septate cystic area. Reviewing the newborn screening database confirmed that a newborn screening for congenital hypothyroidism was done on day 6 of life and TSH was $<$ 0.6 mU/l. She was started on levothyroxine with normalisation of von Willebrand factor antigen levels and coagulation profile within 3 weeks. Later, her periods stopped, her height improved, prolactin normalised, and the ovarian cyst disappeared. This case illustrates the multisystem effects of severe primary hypothyroidism: short stature, coagulation disorders (secondary von Willebrand factor deficiency), pseudoprecocious puberty, high prolactin and ovarian cysts. It also shows the quick resolution of symptoms following the initiation of levothyroxine treatment.

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Thyroid hormone resistance from misdiagnosis to successful pregnancy

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Thyroid hormone resistance is a rare condition, caused by mutations of the thyroid hormone receptor beta (THRB) gene, inherited in an autosomal dominant manner, resulting in decreased tissue sensitivity to thyroid hormone action, leading to high FT4 levels with normal TSH levels. We present a case of thyroid hormone resistance, initially misdiagnosed and treated as hyperthyroidism. An 8 year old girl was referred due to poor appetite, FT4 level was elevated (38.5 pmol/l) with normal TSH (3.47 mIU/l). Due to unusual thyroid function results, she was referred to the paediatric endocrine team. She was thought to be hyperthyroid and commenced on Carbimazole and Thyroxine 'block and replace' regimen. Anti TPO and anti TSH receptor antibodies were negative. Thyroid ultrasound was normal. Follow up thyroid function testing revealed elevated TSH levels and

compliance was queried. She subsequently developed a large goitre over the next 2 years. On review in clinic at the age of 12 years, further questioning revealed a strong family history of thyroid abnormalities. The patient's mother had 'abnormal thyroid tests' which were not treated. Review of her initial results led to a diagnosis of thyroid hormone resistance, which was confirmed on genetic testing (THR beta gene). Medication was discontinued and goitre resolved. The condition was explained to the patient & her guardian. The impact on future pregnancy was discussed. The patient became pregnant at 17 years of age, but had a miscarriage. She became pregnant at 18 years of age and was reviewed at the specialist endocrine antenatal clinic. She was treated with a low dose Propylthiouracil, pending amniocentesis. Fetal genetic testing was negative. Dose of Propythiouracil was adjusted according to TFTs and she had a healthy baby. This case highlights the importance of detailed family history, clinical assessment and consideration of differentials of abnormal thyroid results. Patient education is vital in cases of rare endocrine conditions which can be misinterpreted. The antenatal management of thyroid hormone resistance is discussed.

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Don't make a drama out of a Crisis!

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Introduction

Hashimoto's thyroiditis is the most common cause of acquired hypothyroidism in children and adolescents affecting ten time more females than males. Diagnosis is based on clinical features and antibodies against thyroid peroxidase (TPO) or thyroglobulin (TG). Addison's is an autoimmune disease resulting in primary adrenal insufficiency. It is extremely rare in children and easily misdiagnosed. Levothyroxine may precipitate adrenal crisis in individuals with undiagnosed adrenal insufficiency.

Case Report

A 14 year old girl was referred to Adult Endocrinology with acutely tender diffuse goitre and tiredness. Laboratory results indicated hypothyroidism alongside strongly positive TPO antibodies resulting in the diagnosis of Hashimoto's thyroiditis. No further blood tests were undertaken, and levothyroxine was commenced. 14 weeks later she presented to the Emergency Department with severe lethargy, abdominal pain, anorexia and nausea and vomiting and was referred to the tertiary referral centre (TRC) as a surgical abdomen. On assessment in TRC, she was noted to have metabolic acidosis (pH 7.23), hyponatremia ($Na+$ 121 mmol/l), hypoglycaemia (3.0 mmol/mol) alongside tachycardia (125 bpm) and hypotension (95/57 mmHg) requiring fluid resuscitation (3x10 ml/kg 0.9%NaCl) and dextrose bolus (2x2 ml/kg 10% Dextrose). Blood pressure remained labile despite fluid resuscitation and there was a noted reluctance to continue in light of hyponatremia. On further assessment, significant hyperpigmentation was noted and confirmed not to be fake tan and a diagnosis of adrenal crisis made. Two doses of Intravenous hydrocortisone was administered followed by an intravenous infusion due to limited response. She was referred to the Paediatric Intensive Care Unit (PICU) for inotropic support and ongoing care. Further Endocrine assessment was carried out but all bloods were normal except for very high levels of anti-adrenal antibodies which lead to a diagnosis of Addison's disease. She was discharged home five days later.

Conclusion

Levothyroxine can precipitate adrenal crisis in individuals with undiagnosed adrenal insufficiency due to increased metabolism in the liver. The potential coexistence of adrenal insufficiency should be suspected in patients with diagnosed autoimmune thyroid disease and an early morning cortisol checked prior commencement of levothyroxine.

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