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50th Annual Meeting of the British Society for Paediatric Endocrinology and Diabetes, 2023

8–10 November 2023, Manchester

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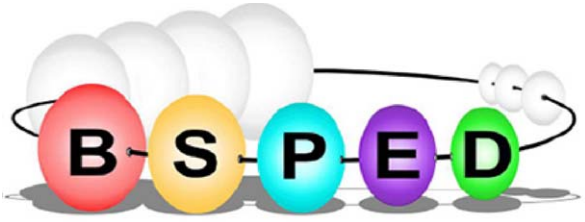

British Society for Paediatric Endocrinology and Diabetes

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Endocrine Main Meeting Sessions

CEW Symposium

CS1.1

Developing & delivering a national service for CEW

Rachael Brandreth[1] & Sarah Jane Blackstock[2]
[1]CYP transformation programme, NHSE, United Kingdom. [2]Clinical Fellow CEW Programme, CYP Transformation team, NHSEI, United Kingdom

The NHS long-term plan made a commitment to annually treating 1000 children and young people living with severe obesity and complications of excess weight. Facilitated by the children's and young people's transformation programme at NHSE this has become a reality. This presentation will talk you through the design and delivery of a national programme unlike any before it.

DOI: 10.1530/endoabs.95.CS1.1

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Endocrine Symposium 1

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Abstract Unavailable

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ES1.2

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How Do I? (Endocrine)

HDI1.1

Abstract Unavailable

DOI: 10.1530/endoabs.95.HDI1.1

HDI1.2

How do I manage metabolic bone disease of prematurity

Amish Chinoy
Royal Manchester Children's Hospital, Manchester, United Kingdom

(ENDOCRINE)Metabolic bone disease of prematurity (MBDP) occurs due to under-mineralisation of the preterm skeleton postnatally, as the baby misses the large amounts of mineral accretion that occurs during the third trimester, coupled with postnatal feeding regimes being unable to replicate this in utero mineral supply. Furthermore, postnatal risk factors such as reduced movements, parenteral nutrition and certain medications can worsen MBDP. If left unmanaged or mismanaged, it can lead to osteopenia, rickets, and eventually fractures. As there are rarely clinical signs of early MBDP, it is identified biochemically on laboratory screening, typically with elevated alkaline phosphatase and reduced serum phosphate. However, it is the plasma parathyroid hormone (PTH) that can help to differentiate between primarily calcipenia (elevated PTH) or phosphopenia (normal PTH), and thus guide treatment. Management should focus on preventative measures, including reducing risk factors and ensuring feeding regimens provide optimal calcium and phosphorus. Prophylactic phosphate supplementation is not recommended, as this can worsen MBDP in a primarily calcipenic state, by worsening the secondary hyperparathyroidism. Where the issue is primarily calcipenia, calcium supplementation will be needed. In primarily phosphopenic state, phosphate supplementation is required, but calcium supplementation may also be needed, to maintain an optimal calcium:phosphorus ratio, which facilitates optimal absorption of these minerals. Controversies remain about the long-term implications of MBDP, and the role of vitamin D. Current research is focused on the use of physical therapies to assist bone development in MBDP.

DOI: 10.1530/endoabs.95.HDI1.2

Debate (Endocrine/Diabetes)

D1.1

Abstract Unavailable

DOI: 10.1530/endoabs.95.D1.1

D1.2

Abstract Unavailable

DOI: 10.1530/endoabs.95.D1.2

Personal Practice Session

PPS

Abstract Unavailable

DOI: 10.1530/endoabs.95.PPS

Diabetes Professionals Day Sessions

Diabetes Symposium 1

DS1.1

Preparing for a softer landing at diagnosis - how to manage a child with pre-T1D

Rachel Besser
Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom

Type 1 diabetes (T1D) can be identified pre-symptomatically, by measuring islet associated autoantibodies (IAb). In an analysis from multiple prospective cohort studies, >80% children with two or more IAbs developed clinical T1D over 15 years of follow up. The reasons for identifying children presymptomatically include reducing the risk of diabetic ketoacidosis at diagnosis and the related morbidity and mortality, reducing the need for hospitalisation, providing time to allow a smoother transition to insulin therapy, and to offer individuals opportunities to trial new treatments to delay T1D onset. Until recently, screening programmes using IAb have been limited to first degree relatives (FDRs), because of the ten-fold increased risk of T1D compared to the general population. However, the knowledge that more than 85% children with T1D do not have an affected FDR, has been a driving force in establishing general population screening programmes globally. Already in the UK children with IAb are being identified by clinical and research teams. However, the benefits of screening can only be realised if linked to a monitoring and follow-up programme. In this talk, we will discuss an approach to managing the child with positive IAb in clinical practice.

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DS1.2

Abstract Unavailable

DOI: 10.1530/endoabs.95.DS1.2

How Do I? (Diabetes)

HDI2.1

Abstract Unavailable

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HDI2.2

Abstract Unavailable

DOI: 10.1530/endoabs.95.HDI2.2

Diabetes Main Day Sessions

Diabetes Symposium 2

DS2.1

Abstract Unavailable

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DS2.2

Abstract Unavailable

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DS2.3

Abstract Unavailable

DOI: 10.1530/endoabs.95.DS2.3

Diabetes Symposium 3

DS3.1

Abstract Unavailable

DOI: 10.1530/endoabs.95.DS3.1

DS3.2

Abstract Unavailable

DOI: 10.1530/endoabs.95.DS3.2

DS3.3

Abstract Unavailable

DOI: 10.1530/endoabs.95.DS3.3

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Endocrine Symposium 2

ES2.1

Abstract Unavailable

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ES2.2

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ES2.4

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Endocrine Symposium 3

ES3.1

Abstract Unavailable

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ES3.2

Abstract Unavailable

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ES3.3

Abstract Unavailable

DOI: 10.1530/endoabs.95.ES3.3

Oral Communications

Oral Communications 1

OC1.1

Swabbing for Staphylococcus in skin reactions to diabetic devices: not a rash decision

Nina Mann[1], Tanya O. Bleiker[1] & Julie Smith[2]
[1]Dermatology Department, University hospitals of Derby and Burton NHS foundation trust, Derby, United Kingdom. [2]Paediatric Department, University hospitals of Derby and Burton NHS foundation trust, Derby, United Kingdom

Devices such as continuous glucose monitoring systems and insulin pumps are being increasingly used, improving quality of life and diabetic control for those with Type 1 diabetes mellitus. Skin reactions can occur at the local site which could be allergic, irritant or infective in nature. The history is key in differentiating between these. Typically infective or irritant dermatitis tend to cause intermittent problems and may start within days of a new device being applied to the skin. Allergic contact dermatitis (ACD) tends to present after months of device use and the problem persists, often meaning patients will have to stop use or use an alternative device. Accurate diagnosis allows individuals to successfully continue using these life changing technologies. We report on two cases in which ACD was considered, however not felt to be entirely typical. After thorough assessment they were found to have carriage of Staphylococcus aureus (S. aureus). Risk factors for S. aureus include diabetes and cannula sites, making these patients high risk. A 14 year old started using Omnipod insulin pump in October 2020, four months later a red itchy rash was noted at the local site, nasal swab was positive for S. aureus, treatment with decolonisation and oral Flucloxacillin was started. The rash persisted until nasal swabs were clear. A second patient started using the Omnipod insulin pump in Aug 2022, three months later an itchy red rash developed, both skin and nasal swabs were positive for S. aureus. Treatment with topical Fucibet and decolonisation cleared the rash, subsequent swabs were negative. Both cases have been able to continue using the devices without further issues. These cases demonstrate that accurate diagnosis can allow effective and timely management of device related rashes and highlight the importance of performing nasal swabs. In our service we routinely perform nasal and skin swabs if there are features that are not typical of ACD and are frequently finding positive nasal carriage and resolution of the problem with decolonisation.

DOI: 10.1530/endoabs.95.OC1.1

OC1.2

45,X/46,XY DSD with gender dysphoria: the conundrum around pubertal induction

Sumana Chatterjee[1], Julie Alderson[1], Zoe Edwards[2], Fiona Mcandrew[2], Cara Williams[2], Urmi Das[2], Karim Awad[1], Julie Park[2] & Dinesh Giri[1]
[1]Bristol Royal Hospital for Children, Bristol, United Kingdom. [2]Alder Hey Children's Hospital, Liverpool, United Kingdom

Introduction
Mixed gonadal dysgenesis (MGD) is a rare form of difference in sex development (DSD) characterised by mosaic karyotype of 45,X/46,XY and dysgenetic gonads. Gender dysphoria can be associated, the frequency of which is unknown. We describe 2 cases of MGD with gender dysphoria and the conundrum around pubertal induction.
Case 1
An 8-year-old, reared as a girl, presented with longstanding concerns about appearance of external genitalia. She was increasingly identifying as a boy. She had clitorophallic enlargement (2 cm), common urogenital sinus and no palpable gonads. Biochemical investigations showed pre-pubertal gonadotrophins, undetectable testosterone, normal urine steroid profile and normal AMH/Inhibin B. The karyotype was 45,X/46,XY. Laparoscopy showed dysgenetic gonads leading to bilateral gonadectomy. The histology did not show evidence of malignancy.
Case 2
A term baby with DSD was noted to have clitoro-phallic enlargement (1.5cm), chordee, urogenital sinus and a left palpable gonad. Karyotype was 45,X/46,XY and female sex of rearing was assigned. Laparoscopy showed a right streak gonad, an abnormal left testis, right hemi-uterus and fallopian tube. Gonadal biopsy did not show any germ cell tissue. Following extensive MDT discussion and parental input, bilateral gonadectomies and clitoral reduction surgery was performed at 11 months. At 3 years, they were displaying tomboy behaviour and subsequently, the patient started identifying as male. They were referred to a specialised gender identity service where they expressed preference of testosterone as the hormone of choice for pubertal induction.
Discussion
The commencement of puberty in these 2 patients who have been raised as females but identify themselves as males during middle childhood, in the absence of gonads will be solely reliant on induction with exogenous sex hormones. Inducing puberty with testosterone in line with childhood gender identity, may pose ethical dilemmas as they are not of legal consent-giving age. Waiting until legal consent age can potentially entail a risk of significant psychosocial and sexual issues surrounding delaying puberty. Case 2 had a clitoral reduction, which poses a further challenge to gender reassignment in terms of possible surgical outcomes in the future, which may influence decision making regarding hormonal induction of puberty.

DOI: 10.1530/endoabs.95.OC1.2

OC1.3

Hyperpigmentation related to diabetes technology adhesives: an unusual presentation of Addison's disease in a child with type 1 diabetes mellitus

Rebecca Moon[1,2,3], Amy Rowland[2] & Justin Davies[1,4]
[1]Paediatric Endocrinology, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom. [2]Paediatric Diabetes, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom. [3]MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, United Kingdom. [4]Faculty of Medicine, University of Southampton, Southampton, United Kingdom

Background
Children with type 1 diabetes mellitus (T1DM) are at increased risk of other autoimmune conditions including thyroid, coeliac and Addison's diseases. Hyperpigmentation is a recognized feature of Addison's disease. We present a case with unusual diabetes-technology related hyperpigmentation.
Case report
A 12-year-old male with known T1DM (glutamic acid decarboxylase antibody positive), coeliac disease and autism reported skin darkening at his T-slim insulin pump cannula and Dexcom G6 continuous glucose monitor (CGM) sites. The areas of hyperpigmentation matched the adhesive dressing areas. The skin was not inflamed, hot to touch, raised or tender. Similar areas were visible at previous dressing sites with various shades of brown; he described fading over weeks to months. He had previously been diagnosed with allergic contact dermatitis to the cannula and CGM dressings by dermatology but continued to use them. He also had hyperpigmentation over his knuckles and on the facial skin surrounding his mouth, but not on the buccal mucosa or tongue. There were no symptoms of adrenal insufficiency. He was gaining weight and height, following the 98th and 75th centiles, respectively. His glycaemic control was suboptimal (time in range 42%, HbA1c 66mmol/mol). Notably, he had borderline low plasma sodium (128-132mmol/l) for 12 months. An urgent synacthen test showed a peak cortisol of 370nmol/l with a raised adrenocorticotrophin hormone (ACTH) of 76ng/L, confirming primary adrenal insufficiency. His plasma sodium and potassium were 132mmol/l and 4.8mmol/l, respectively, with an aldosterone of 298pmol/L and renin of 660mU/L, consistent with early mineralocorticoid deficiency. Adrenal antibodies were positive.
Discussion
Hyperpigmentation is recognized to occur in primary adrenal insufficiency due to increased melanocyte stimulating hormone from the formation of ACTH. This typically occurs in the buccal mucosa and skin exposed to pressure, for example the knuckles and skinfolds, and trauma. Hyperpigmentation at sites of diabetes technology adhesives has not previously been described. Localized skin trauma from adhesive dressing removal or, in this case, allergic dermatitis might have contributed. Importantly, hyperpigmentation at sites of diabetes technology dressings should not be assumed to be related to allergic dermatitis; Addison's disease should be considered, and urgently excluded.

DOI: 10.1530/endoabs.95.OC1.3

Oral Communications 2

OC2.1

A novel maternally inherited GNAS variant in a family with hyperphagia and obesity

Preetha Purushothaman[1], Dillon Popat[2], Anand Ramakrishnan[1], Li Chan[2] & Evelien Gevers[1,2]
[1]Department of Paediatric Endocrinology Barts Health NHS Trust - Royal London Children's Hospital, London, United Kingdom. [2]Centre for Endocrinology William Harvey Research Institute Barts and The London

School of Medicine and Dentistry Queen Mary University of London, London, United Kingdom

Introduction
Heterozygous inactivating mutations in the maternal allele of the GNAS gene typically result in pseudohypoparathyroidism (PHP). GNAS variants were recently described in 1% of patients, not known to have PHP, in the UK Genetics of Obesity cohort, resulting in reduced MC4R signalling and variable effects on PTH-R and GHRH-R signalling.
Methods
NGS (Cambridge Obesity Gene Panel) and *in vitro* functional analysis using cAMP biosensor assays.
Case
A six-year-old female (BMI +4.3SD, height +1.9SD) presented with hyperphagia and obesity from age 3. She had subtle brachydactyly. Developmental milestones were mildly delayed. Her 12-year-old brother (height +2.1SD, BMI +2.9SD) was followed in an obesity clinic and had hyperphagia, obesity, mildly delayed development and autism, with progressing puberty. He had subtle brachydactyly, as did the mother (BMI 38.9kg/m2, height 160.2cm).
Results
In the proband, PTH was mildly raised [9.5 pmol/L (0.7-5.6)] with normal calcium and Vitamin D; TSH 6.6 mU/L (<6), FT4 11.8 pmol/L (10.8-19.0). The brother and mother had mildly raised PTH but otherwise normal endocrinology. Brother's bone age was 3 yrs advanced. A novel heterozygous (c.791A>C, p.(Asn264Thr) variant in exon 10 of GNAS was detected in the proband, mother and brother. The variant is in a highly conserved region and has been classified as pathogenic (ACMG and ACGS), and is not present in control databases. Functional effect of p.(Asn264Thr) was assessed by heterologously expressing GSWT or GSAsn264Thr in HEK293 cells, together with GPCRs 3xHA-GHRHR, 3xHA-MC4R or 3xHA-PTHR. After stimulation with GHRH, α-MSH and PTH, cAMP generation was significantly impaired in GSAsn264Thr compared to GSWT, supporting the pathogenic nature of the variant for all 3 signalling pathways.
Discussion
GNAS variant p.Asn264Thr leads to impaired MC4R, GHRH-R and PTH-R signalling *in vitro* but a clinical presentation dominated by obesity without a classical PHP phenotype. The obesity may compensate for the impaired GHRH-R signalling resulting in normal growth in height although pubertal growth could still be impaired. Patients with obesity should be assessed for subtle clinical and biochemical features of PHP for early diagnosis. Whether Setmelanotide is effective in improving MC4R signalling in these patients remains unanswered currently.

DOI: 10.1530/endoabs.95.OC2.1

OC2.2

Conquering the Storm: Surgical Intervention Rescues an Adolescent girl with Severe Thyrotoxicosis Refractory to Medical Management

Sajili Mehta, Pon Ramya Gokul, Raj Ankur, Katherine Lau, Julie Park & Poonam Dharmaraj
Alder Hey Children Hospital, Liverpool, United Kingdom

Introduction
Graves' disease (GD), although the most common cause of hyperthyroidism, is relatively uncommon in children, usually manifesting insidiously. Thyroid storm is a well described but rarely seen phenomenon in childhood GD; thyrotoxic crisis is less often discussed and its management can be challenging. We describe a case of GD with thyrotoxic crisis.
Case
A 14-year-old female, known to have inadequately controlled GD for one year, recently relocated to the UK. She presented with acute breathlessness and change in voice and was found to be tachycardic, hypertensive and agitated with significant exophthalmos and large goiter, consistent with thyrotoxic crisis. Acute management with propylthiouracil, propranolol and intravenous hydrocortisone stabilized her but free T4 and T3 levels were unrecordably high for 10 days. Deterioration in liver function necessitated switching to carbimazole, the dose of which was maximized over the next 2 weeks and cholestyramine added to her regimen. Thyroidectomy was planned and Lugol's iodine commenced, but in view of persistent high free T3 levels with tachycardia and hypertension, it was felt that further optimization of her management was required before surgery could be undertaken safely. Hydralazine and dexamethasone finally brought her blood pressure and thyroid function under control. Lugol's iodine, which had been stopped, could not be safely restarted prior to surgery in view of its potential detrimental effect on thyroid hormone production. 6 weeks after initial presentation, she was significantly better with free T4 and T3 in the normal range for the first time and improvement in cardiovascular parameters as well as symptoms. She underwent thyroidectomy without complications. Anticipated thyroid storm in the immediate post-operative period did not occur and hypocalcemia was managed with intravenous calcium and alfacalcidol. She was discharged on levo-thyroxine and continues to be monitored closely.
Conclusion
Thyrotoxic crisis complicating pediatric GD is challenging to manage, requires a robust understanding of the different drug treatments and particular attention to the cardiovascular and hemodynamic effects of the toxic state. Our patient required multidisciplinary management between physicians, surgeons, anesthetists and ophthalmologists as well as critical care monitoring in the post-operative period when thyroid storm may still occur.

DOI: 10.1530/endoabs.95.OC2.2

OC2.3

Hypopituitarism – a rare manifestation in Joubert syndrome: About 4 cases

Elżbieta Marczak[1], Maria Szarras-Czapnik[1], Elżbieta Moszczyńska[1], Małgorzata Wójcik[2], Agata Zygmunt-Górska[2], Jerzy Starzyk[2], Karolina Czyżowska[3] & Agnieszka Zachurzok[3]
[1]Department of Endocrinology and Diabetology, The Children's Memorial Health Institute, Warsaw, Poland. [2]Department of Pediatric and Adolescent Endocrinology, Chair of Pediatrics, Pediatric Institute, Jagiellonian University Medical College, Krakow, Poland. [3]Department of Pediatrics, Endocrinology and Diabetes, Medical University of Silesia, Katowice, Poland

Introduction
Joubert Syndrome (JS) is a rare ciliopathy condition, presenting distinctive cerebellar and brain stem malformation called the "molar tooth sign" (MTS) on brain imaging. Patients suffer from neonatal breathing dysregulation, developmental delay, hypotonia, abnormal eye movements. Endocrine disorders are only rarely evaluated, to date only few reports highlight the importance of hormonal evaluation.
Materials and methods
We report 4 cases of endocrine deficiencies in JS. Our series consisted of 3 boys and a girl. Endocrine evaluation was based on assessment of thyroid and adrenal function, serum levels of insulin-like growth factor 1 (IGF-1), IGF binding protein 3 (IGFBP-3), gonadotropins and testosterone.
Results
2 boys were born with micropenis, basal testosterone levels were low, therefore in each case 3 doses of testosterone were administered at a monthly interval, starting at 3 months old. Treatment correlated positively with penile growth. Suspicion of GHD was based on undetectable levels of IGF-1 and in one case episodes of hypoglycaemia. Two children required early recombinant human growth hormone (rhGH) treatment. Hypothyroidism was confirmed in all cases, treated with l-thyroxine. Adrenal insufficiency was present in 3 cases. Therapeutic management consisted of hydrocortisone.
Conclusion
Joubert syndrome is multisystem disorder that may be variable with presentation Our goal was to emphasize the role of endocrine system disorders as the awareness of this condition is essential for appropriate intervention.

DOI: 10.1530/endoabs.95.OC2.3

Oral Communications 3

OC3.1

The first description of an MC4R variant in a patient with Kallmann syndrome and obesity

Aisha A Aslam[1], Sharon Lim[2], Ruben Willemsen[1], Sasha R Howard[1,3] & Evelien Gevers[1,3]
[1]Department of Paediatric Endocrinology, The Children's Hospital at the Royal London Hospital, London, United Kingdom. [2]Broomfield Hospital, Chelmsford, United Kingdom. [3]William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University, London, United Kingdom

Introduction
Pathogenic MC4R variants result in hyperphagia and early onset obesity but puberty is not usually affected. We describe an MC4R variant in a patient with Kallmann syndrome and obesity.

Case
A 16 year old male with repaired Tetralogy of Fallot, anosmia, autism and anxiety, was referred with obesity and delayed puberty. Height was -1.31 SDS, BMI 30.7 kg/m2. He had a high arched palate, normal skin, normal hair colour, mild hypertelorism and upward slanting palpebral fissures. Pubertal staging was A2P1G1 5ml testes.
Results
LHRH test showed borderline low peaks (LH 5.0U/L, FSH 2.55U/L) and inhibin B 108pg/mL (25-325pg/mL). MRI brain showed hypoplastic olfactory bulbs and normal pituitary anatomy. CGH microarray, karyotype and R148 hypogonadism gene panel were normal. He underwent whole genome sequencing in the Genetic Factors Affecting the Timing of Puberty Study; no abnormalities in known genes associated with GnRH deficiency were found but detected a previously described heterozygous variant, MC4R c.542G>A, p.Gly181Asp, classified as pathogenic and not present in control databases.
Management
He was commenced on Testosterone but showed progression of testicular size to 10mL and testosterone was stopped but required restarting. Repeat investigations off treatment (aged 22 years, testes 15mL): inhibin B 66pg/mL, testosterone 2nmol/L, baseline LH 2.4U/L, stimulated peak 24.9U/L, baseline FSH 1.2U/L, stimulated peak 4.2U/L.
Discussion
Previous *in vitro* work has shown complete loss of function of MC4R p.Gly181Asp due to reduced binding to a-MSH and reduced cell surface expression. Heterozygous p.Gly181Asp have been described in several children/-adults with obesity; but hypogonadism in heterozygous carriers has not. Homozygous MC4R p.Gly181Asp was found in a male with obesity and partial HH thought to be due to abnormal GnRH production but with normal olfactory bulbs. We are the first to describe a heterozygous MC4R p.Gly181Asp variant in a patient with partial hypogonadism and anosmia with hypoplastic bulbs in addition to obesity. Interaction between POMC-MC-leptin circuits and Kisspeptin-GnRH circuits is recognised although not completely understood. Our results support a role for MC4R in GnRH secretion and potentially olfactory cell/GnRH neurone migration. Screening for MC4R should be considered in cases of hypogonadism and early onset obesity.

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OC3.2

Lessons learned from a case of fungal candida thyroiditis: a rare but serious condition

Rachel Varughese, Sinead McGlacken-Byrne, Alison Conlon, Catherine Peters & Antonia Dastamani
Great Ormond Street Hospital, London, United Kingdom

Introduction
Disseminated fungal disease is an opportunistic infection mostly seen in immunocompromised patients, however, fungal thyroiditis in this context is rare, with few previously reported cases (predominantly Aspergillus, only one case of paediatric candida thyroiditis). We present a case of Candida tropicalis induced thyroiditis, to highlight this rare (likely underreported) cause of thyroid disease.
Case
A 9-year-old female was diagnosed with acute lymphoblastic leukaemia (ALL). Admission cultures confirmed Candida tropicalis in stool and urine. On day 12 of induction, she developed febrile neutropenia, treated with antifungals and antibiotics. Around this time, she also developed steroid-induced diabetes and thyroid function (TFTs) revealed mild hyperthyroidism: T4-23.7pmol/L, TSH-0.35mU/L. 2 weeks later, she developed a fever recurrence. High-beta glucan levels suggested disseminated fungal infection. A leg nodule biopsy demonstrated fungal hyphae, with Candida tropicalis, confirmed on PCR and fungal culture. Retrospectively, multifocal parenchymal abnormalities were noted in an earlier renal ultrasound consistent with fungal infiltrates. 3 weeks later, in the setting of ongoing fevers and tremors, repeat TFTs confirmed hyperthyroidism (free T4-68.5pmol/L, TSH<0.02mU/L). Thyroid ultrasound: 'irregular hypoechoic area, similar in configuration and detail to that demonstrated in the right calf, consistent with fungal lesion'. Thyroid NM pertechnetate scan: no significant tracer uptake, consistent with thyroiditis Antibodies: TRAb and TPO negative. Our patient received fluconazole and caspofungin, with ambisome introduced due to suspected resistance. She initially received propanol, while risks of neutropenia with carbimazole were debated in the oncological context. Symptoms continued and carbimazole and prednisone were added, following which fevers and tachycardia rapidly resolved.
Key Learning
- Candida fungal thyroiditis is rare, requiring a high index of suspicion in the setting of immunocompromise
- Fungal thyroiditis symptoms overlap significantly with those of sepsis or underlying oncological diagnoses that many fungal-susceptible patients carry. Our patient presented with fever, tachycardia, weight loss and tremors. Neck pain was not a feature, but on direct questioning, dysphagia was evident
- Rapid diagnosis aids timely introduction of antifungal and anti-thyroid medication
- Our patient had a 'herald' leg nodule biopsied and was later found to have similar renal and thyroid lesions on imaging, sparing her the need to undergo further, more invasive biopsies.

DOI: 10.1530/endoabs.95.OC3.2

OC3.3

A complex case of pituitary gigantism: overcoming challenges in diagnosis and treatment

Manju Chandwani[1], Anbezhil Subbarayan[1], Miles Levy[1] & Marta Korbontis[2]
[1]Leicester Royal Infirmary, Leicester, United Kingdom. [2]Queen Mary University of London, London, United Kingdom

A 4.9-year-old girl presented with symptoms suggestive of early puberty and rapid growth. Her medical history revealed that she had been a tall child since infancy. Family history was notable for Lynch syndrome in her father and paternal grandmother. Upon examination, the patient was pre-pubertal but had a height of 124 cm (SDS 3.5) and a height velocity of 15 cm/year. Further investigations revealed elevated levels of IGF-1, IGFBP3, and failed GH suppression on an OGTT, indicating a potential somatotropinoma. Imaging with contrast MRI confirmed the presence of a pituitary microadenoma, leading to referral to paediatric neurosurgery and geneticist. At the age of 5.66 years, the patient underwent a trans-sphenoidal excision of the microadenoma with intra-operative MRI guidance. Histology confirmed the presence of a neuroendocrine tumor expressing growth hormone. Post-surgery, her height velocity and IGF-1 levels decreased, indicating a positive response. However, subsequent monitoring revealed a rise in IGF-1 levels, suggesting incomplete resection or recurrence. Repeat imaging with contrast MRI and 11C-Methionine PET scan confirmed the presence of a small residual adenoma in the pituitary gland. In light of this, the patient has been initiated on Pegvisomant therapy, which has resulted in rapid decline in IGF-1 levels. A repeat MRI scan is planned to determine the need for further surgery. Genetic testing using the R217 gene panel has shown normal results, but the results of X-linked acro-gigantism genetic testing are still pending. The family has expressed reluctance for the patient to undergo genetic testing for Lynch syndrome, although the association of corticotroph and prolactin-secreting adenomas with Lynch syndrome has been noted. Discussions regarding the importance of genetic testing for Lynch syndrome are ongoing with the family. Currently, the family faces a decision between long-term Pegvisomant therapy, provided the tumor remains under control, or pursuing repeat surgery, which carries a high risk of subsequent pituitary hormone deficiencies. The case highlights the challenges encountered in managing children with somatotropinomas, emphasizing the importance of multidisciplinary care and close monitoring to optimize treatment outcomes. The collaborative efforts of paediatric endocrinologists, neurosurgeons, and geneticists are crucial in ensuring appropriate diagnosis, treatment, and follow-up care.

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Oral Communications 4

OC4.1

Cortisone reductase deficiency: a rare cause of hyperandrogenaemia and premature adrenarche

Kyriacos Gregoriou, Preetha Purushothaman & Claire Hughes
Department of Paediatric Endocrinology Barts Health NHS Trust - Royal London Children's Hospital, London, United Kingdom

Introduction
11-beta-dehydroxysteroid dehydrogenase-1 (11BHSD1) is a bidirectional enzyme which converts inactive cortisone and 11-dehydrocorticosterone to active cortisol and corticosterone and vice-versa. The direction is dependent on NADPH availability and the action of the cofactor enzyme hexose-6-phosphate dehydrogenase (H6PDH). Cortisone reductase deficiency is a rare disorder caused by defects in 11BHSD1 or H6PDH, leading to inability to regenerate active glucocorticoid. This condition is characterised by increased cortisol metabolic clearance, stimulating ACTH mediated adrenal hyperandrogenism. Here, we

present the case of an 8 year old boy with 11BHSD1 deficiency who presented with premature adrenarche.
Case
An 8.1 year old boy presented with a 6-12 month history of increasing body odour, axillary and pubic hair. Auxology showed height was 134.9 cm (SDS: +1.19), weight 31.6 kg and BMI 17.98 kg/m2. Tanner staging P2A2G1 and testicular volume 3ml were consistent with premature adrenarche.
Results
Investigations showed elevated adrenal androgens: DHEAS 5.1umol/l (0-0.4 umol/L), androstenedione 0.8 nmol/L (0—0.4 nmol/L). Synacthen test showed adequate response with peak cortisol 667 nmol/L and normal 17-OHP. Gonadotropins were in the prepubertal range (FSH- 1.5 U/L, LH <1.0 U/L) with testosterone <1.0 nmol/L. Growth hormone, IGF-1 and thyroid function were normal. Bone age was significantly advanced. At chronological age 8.1 years, Greulich and Pyle bone age was 11.6 years and Tanner-Whitehouse 10.8 years (+3.85 SD). Urine steroid profiles showed a very low ratio (0.07) of cortisol (11-hydroxy) to cortisone (11-oxo) metabolites (NR age 6-8 years; mean ratio 0.7 with SD 0.2) confirming 11BHSD1 deficiency. Genetic testing for mutations in HSD11B1 and H6PD genes is pending.
Conclusions
Urine steroid profiling (USP) has identified 11BHSD1 deficiency as a rare cause of premature adrenarche in this child. This defect is causing ACTH mediated excess adrenal androgens as illustrated by high DHEAS resulting in premature adrenarche with significantly advanced bone age. There are very few other cases reported in the literature and minimal experience regarding potential treatment options to alleviate the hyperandrogenaemia. Currently we have not initiated treatment but are closely monitoring his progress. This case illustrates the benefit of USP in cases of premature adrenarche.

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OC4.2

A deletion at 20p11.21 region involving *FOXA2* causing Congenital Hyperinsulinism and extra pancreatic features

Katherine Hawton[1,2], Stuart Nath[3], Yadlapalli Kumar[3] & Dinesh Giri[1,2]
[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom. [2]University of Bristol, Bristol, United Kingdom. [3]Royal Cornwall Hospitals NHS Trust, Truro, United Kingdom

Introduction
Congenital hyperinsulinism (CHI) is a rare disease characterized by an unregulated insulin release, leading to hypoglycaemia. It is the most frequent cause of persistent and severe hypoglycaemia in the neonatal period and early childhood. *FOXA2*, a beta-cell transcription factor is localized at the cytogenetic location 20p11.2 and is critical for the development of pancreas and pituitary gland. We describe a child with 20p11.21 deletion encompassing heterozygous whole gene deletion *FOXA2* causing congenital hyperinsulinism with potential pituitary involvement.
Case
Our patient, a 3-year-old girl, was born to non-consanguineous parents at 39-week gestation with a birth weight of 2.82 kg presented with seizures at 45 hours of age. Her blood glucose was <0.3mmol/L with an inappropriately elevated plasma insulin of 209pmol/L and an inappropriately supressed β- hydroxybutyrate and free fatty acids consistent with the diagnosis of CHI. Her maximum glucose infusion rate was 20mg/kg/minute. She responded to diazoxide with a maximum dose of 9mg/kg/day. Further investigations included a CGH microarray which showed a 8.3Mb deletion of the short arm of chromosome 20 at 20p12.1p11.21. As this area encompasses *FOXA2*, subsequent tests confirmed a heterozygous *FOXA2* whole gene deletion arising de-novo. Extra pancreatic features in our patient include a subtle dysmorphism, ventricular septal defect, horseshoe shaped kidney and developmental delay involving speech. The baseline pituitary screen included a normal cortisol of 402 nmol/L and normal thyroid function test. During the recent clinic review, at the age of 3, she continues to require diazoxide at a dose of 7 mg/kg/day. Her height velocity was noted to have declined to the 3rd centile with a low IGF1 which is likely to be an evolving growth hormone deficiency. A growth hormone stimulation test and an MRI pituitary gland to look for any structural pituitary abnormalities is being planned.
Discussion
Deletions involving the cytogenic location 20p11.2 band can cause hyperinsulinism as this area encompasses *FOXA2*. The phenotype can extend to affect the pituitary gland and hence regular assessment of pituitary function along with imaging to look for pituitary structural anomalies is important.

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OC4.3

Primary adrenal insufficiency with muco-candidiasis- a rare cause of familial glucocorticoid deficiency due to thioredoxin reductase deficiency

Shaju Edavana[1], Anurag Bajpai[2], Emma Hawkes[1] & Uma Kumbattae[1]
[1]Royal Stoke University Hospital, Stoke ON Trent, United Kingdom. [2]Paeditaric Endocrine Research Center, Kanpur, India

A 11-year 10-month boy born of non-consanguineous marriage presented with recurrent oral and respiratory tract infections and failure to thrive from the age of one year. He was born at term with a birth weight of 3.5 kg with an uneventful perinatal period. The parents noticed recurrent oral infections with the whitish curd-like layer deposited over the oral mucosa. They also complained of gradual skin darkening, easy fatiguability, and growth failure over the last three years. On examination, he was short (height 125 cm;-3.06 SDS), and lean (29.3 kg,-1.23 SDS, BMI 18.7 kg/m2, 0.8 SDS). He had stage 1 pubic hair with a stretched penile length of 4.5 cm and a testicular volume of 1 ml. He had generalized pigmentation with oral candidiasis. Blood pressure was 90/70 mmHg measured in the right arm. The diagnostic work-up showed hyponatremia (serum sodium level of 121 mmol/l; 135-145 mmol/l), and normal potassium (4.2 mmol/L, 3.5-4.5 mmol/l). Cortisol levels were low for the level of hyponatremia (115 nmol/L). Further work-up showed elevated ACTH 379 pg/ml and plasma renin (74.29 pg/ml). A diagnosis of isolated glucocorticoid deficiency due to Familial glucocorticoid deficiency was considered in view of hyponatremia, normal potassium, low cortisol, and high ACTH levels. The boy was started on oral hydrocortisone and a low dose of fludrocortisone. Clinical exome sequencing showed a heterozygous, stop gain mutation in TXNRD2 (c.1341T>G; (p.Tyr447Ter) within exon 15, and compound heterozygous variants were found in the ATP7B gene in exon 2 (c.174dup; (p.Thr59HisfsTer19) and exon 18 (c.3741C>G; (p.His1247Gln).TXNRD2 is a dimeric NADPH-dependent flavin adenine dinucleotide-containing enzyme that catalyzes the reduction of the active disulfide of thioredoxin 2 and other substrates.TXRD2 protects the cell from oxidative stress. The higher production of cortisol, explains the susceptibility of the zona fasciculata to oxidative stress; hence, individuals with TXNRD2 and NNT mutations primarily develop glucocorticoid deficiency. Absence of TXNRD2 in humans leads to glucocorticoid deficiency. Reaching a specific diagnosis can have implications for management and for monitoring associated features, as well as for counselling families about recurrence risk in siblings and relatives.

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Oral Communications 5

OC5.1

Endocrine outcomes in bardet-biedl syndrome from a large single-centre paediatric multidisciplinary clinic

Rachel Varughese[1], Divya Pujari[1], Elizabeth Hatton[2], Theodora Dyakova[3], Kathryn Sparks[4], Sarah Flack[1], Elizabeth Forsythe[4], Phil Beales[1] & Alexander Chesover[1]
[1]Great Ormond Street Hospital, London, United Kingdom. [2]University of Oxford, Oxford, United Kingdom. [3]Barts and The London School of Medicine and Dentistry, London, United Kingdom. [4]National Bardet-Biedl Syndrome Services, London, United Kingdom

Introduction
Bardet-Biedl Syndrome (BBS) is a rare, autosomal recessive ciliopathy, with a prevalence of 1 in 100,000–160,000, caused by mutations across >20 known genes encoding for proteins responsible for primary cilium/basal body complex integrity. Endocrinopathies associated with BBS include hypogonadism, hypothyroidism, and the metabolic complications of obesity. The endocrine characteristics of a large adult BBS cohort have been reported; however, there are fewer data reported in paediatric populations.
Objective
To describe the prevalence of endocrinopathies in BSS from a large paediatric cohort at a single-centre multidisciplinary service.
Method
A retrospective 13-year study of paediatric patients (<18 years) with genetically confirmed BBS at a single-centre paediatric multidisciplinary service. Patient data were collected from electronic records and an independent database. The study was registered and approved by the Hospital Trust.
Results
Of 163 patients seen in the paediatric BBS clinic, 139 (50% female) had genetic confirmation and were included in analysis.Mutations in BBS1 and BBS10 were most common, in 34% and 22%, respectively. Patients overweight/obese (BMI > 1.34 SDs) totalled 128/136 (94%), and 110/136 (81%) were obese (BMI >2.05

SDs). Of patients >16 years, 26/30 (87%) were overweight/obese and 22/30 (73%) were obese.Type 2 diabetes was diagnosed in 3/139 (2%). Metformin was prescribed for 4/129 (3%) patients; two for diabetes, two for impaired glucose tolerance, and one for obesity.For patients >16 years, no patients had needed sex steroid treatment – all had spontaneous onset of puberty and no pubertal arrest. Of males, 8/39 (21%) had delayed puberty. Of females, 3/41 (7%) had delayed puberty, with mean menarche 12.9 years.Thyroid abnormalities were clinical hypothyroidism (on levothyroxine) in 2/125 (2%), subclinical hypothyroidism in 1/125 (1%), and 9/125 (7%) had abnormal thyroid function that self-resolved.
Conclusion
This is the largest analysis of endocrine outcomes for paediatric patients with BBS. Despite dietetic input in an MDT clinic, obesity remains a significant morbidity. Hypogonadism, hypothyroidism, and insulin resistance were not significant morbidities in this cohort and more prevalent in reports from adults. Longitudinal analysis of growth is ongoing. Longitudinal studies into adulthood to better understand timing of endocrinopathies could benefit service development and patient education.

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OC5.2

Gonadotropin treatment for the induction or completion of puberty for males with hypogonadotropic hypogonadism; Two Centre Experience

Dr Kyla Ng Yin[1], Professor Leo Dunkel[1], Dr Claire Hughes[2], Dr Tony Hulse[3], Dr Evelien Gevers[1,2], Mr Lee Martin[2], Dr Rathi Prasad[1,2], Dr Ruben Willemsen[1,2], Professor Gary Butler[4,5] & Dr Sasha Howard[1,2]
[1]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom. [2]Department of Paediatric Endocrinology, Royal London Children's Hospital, Barts Health NHS Trust, London, United Kingdom. [3]Evelina Children's Hospital, London, United Kingdom. [4]Department of Paediatric and Adolescent Endocrinology, University College London Hospital NHS Foundation Trust, London, United Kingdom. [5]UCL GOS Institute of Child Health, University College London, London, United Kingdom

Background
Hypogonadotropic hypogonadism (HH) is a key cause of absent, partial, or arrested puberty. Individuals with HH experience central disorders of the hypothalamic-pituitary-gonadal (HPG) axis, with deficiency in gonadotropin-releasing hormone (GnRH). This leads to inadequate pituitary gonadotropins (luteinising hormone (LH) and follicle-stimulating hormone (FSH)), resulting in immature gonadal development. It has substantial consequences including infertility and reduced quality of life. The mainstay of current therapy is testosterone which facilitates secondary sexual characteristics; however, spermatogenesis is only possible with gonadotropins.
Objective
To evaluate the efficacy of gonadotropin treatment to induce puberty in males with HH as per the local guidelines available on the BSPED website[1]. To investigate the outcomes of treatment, using pre-treatment with recombinant (r) FSH for individuals with severe HH, followed by combined rFSH and human chorionic gonadotropin (hCG), and hCG +/- rFSH for patients with partial HH (defined by baseline TV >6ml).
Design
Retrospective analysis conducted on medical records of males diagnosed with HH who received gonadotropin treatment in two large tertiary hospitals (Royal London Hospital and University College London Hospital) from 2011 to 2023.
Outcome Measures
Primary outcome assessed was testicular volume (TV). Secondary outcomes include semen analysis.
Results
A total of 23 males with HH were included, of which 5 have Kallmann syndrome and 2 have HH post-craniopharyngioma. Mean age at start of gonadotropin treatment was 16.89 (± 2.39) years old. 16 patients received pre-treatment with FSH and subsequent hCG/rFSH, and 7 patients received treatment with hCG/rFSH started simultaneously. Mean TV increased from 3.14ml (± 1.74) to 11.63ml (± 5.21) in the group treated with pre-FSH and increased from 7.33ml (± 2.75) to 14.13ml (± 3.71) in the group treated with hCG/FSH. 11 out of 15 males who completed therapy successfully banked sperm. Therapy was well tolerated with only 1 patient choosing to discontinue treatment.
Conclusions
Gonadotropin treatment was effective in inducing or completing puberty in males with HH. Our clinical practice suggests that pre-FSH treatment is a viable option for individuals with TV <6ml, resulting in significant increase in TV. Further prospective studies are warranted to validate these findings and establish standardised treatment guidelines.

[1] BSPED, 2021. https://www.bsped.org.uk/media/1989/protocol-for-induction-of-puberty-with-gonadotropins-in-males-with-gnrh-or-gonadotropin-deficiency_bsped_website-002.pdf

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OC5.3

Origins of the lower vagina and the role of androgens from 20 years' experience with genitoplasty for 46XX classical congenital adrenal hyperplasia (CAH)

Supul Hennayake, Anju Goyal, Piotr Hajduk & Leena Patel
Royal Manchester Children's Hospital Manchester, Manchester, United Kingdom

Based on the traditional belief that the lower vagina does not form owing to excess androgens in utero, extensive dissections are undertaken to bring the vagina down to the skin level in 46XX CAH individuals. However, long held knowledge about the embryological origins of the lower vagina and the key role of androgens has been questioned by genetic and molecular studies [Cai Y. 2009. https://doi.org/10.1387/ijdb.082846yc]. Our aim was to assess the level of the vaginal introitus (VI) in relation to the perineal body (PB) in 46 XX CAH.
Methods
Urogenital anatomy was prospectively studied during feminising genitoplasty in all consecutive 46XX CAH subjects by the first author from January 2003 to June 2023. Lengths of clitoris, common channel (CC), vagina and urethra were measured. Level of the VI in relation to the PB and presence of hymen were checked. Patients were categorised by appearance of the CC and VI: Type 1 - CC bifurcating to urethra and vagina; type 2 - CC was indistinguishable from a male urethra and VI was found at the 'verumontanum', sometimes with difficulty.
Results
38 patients were included: 18% were Prader 5 and 76% were Prader 3 or 4. Median age at surgery was 20 months (range 4 months to 16 years). Median vaginal length was 45mm (range 35-65mm) and 89% had a hymen. Age adjusted urethral length was only 3mm shorter in Type 2 than Type 1 ($P=0.017$). Division of fused labial and genital folds was sufficient to expose the VI just in front of PB in all patients. In Type 2 patients, bulbo-spongiosus muscle had to be opened back to the PB and narrow VI had to be opened posteriorly for about 5mm. None required urogenital sinus mobilisation.
Conclusion
In all patients with 46 XX classical CAH, the whole vagina is present, the VI is located at the normal position at the level of the perineal body, and potentially harmful vaginal mobilization is not required. This study provides further evidence that the whole vagina is derived from Mullerian ducts and the role of androgen deficiency on formation of the vagina is a myth.

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OC5.4

A survey of current clinical care of children and young people with Klinefelter Syndrome in United Kingdom

Manju Chandwani[1], Dhivyalakshmi Jeevarathnam[2] & Pooja Sachdev[2]
[1]Leicester Royal Infirmary, Leicester, United Kingdom. [2]Queen's Medical Centre, Nottingham, United Kingdom

The European Academy of Andrology (EAA) published the first consensus guideline on KS in 2021 to standardise the care provided to patients with Klinefelter Syndrome (KS) in various developmental stages. We conducted an online national survey advertised in the British Society of Paediatric Endocrinology and Diabetes newsletter (BSPED) to evaluate clinical care provided to children and young people (CYP) with KS. The survey ran over a period of 4 months (January-April 2023). We received 16 responses out of 22 specialist centres (response rate 72.7%). Majority of the respondents are paediatric endocrinologists (PE) (12, 75%), 2 endocrinology registrars and 2 paediatricians with interest in endocrinology. The lead responsibility for ongoing care of CYP with KS is taken by PE in 2/3rd of centres (rest Community Paediatricians) The commonest age at which CYP with KS are referred to a PE is 11-13 years. The reasons for referral to a PE in a decreasing order are gynaecomastia, delayed puberty, cryptorchidism, behavioural issues, delayed speech and tall stature. Local guidelines for management of KS CYP are available to 62.5% of respondents. When local guidelines are unavailable, clinicians refer to EAA guideline, UpToDate, Medscape, etc for management decisions.

Table showing annual clinical/biochemical tests and the number of respondents undertaking them.

Test/examination	Number (%)
Weight/height and pubertal assessment	16 (100)
Blood pressure	5 (31.3)
Learning difficulties assessment	5 (31.3)
LH, FSH, Testosterone	14 (87.5)
Oestrogen	6 (37.5)
HbA1c, Lipid profile, Thyroid autoimmunity	10 (62.5)
Vitamin D, bone profile	9 (56.3)
Inhibin B, AMH	8 (50)
Testicular ultrasound	2 (12.5)

Some clinicians perform Inhibin B/AMH at the start of pubertal induction, while others only prior to fertility assessment referral. Testosterone is started when a KS young person has raised LH with low testosterone by 12 (75%), slow pubertal progression by 10 (50%), delayed puberty by 9 (56.3%) and raised LH with normal testosterone by 3 (18.8%) respondents. 81.3% follow a transitional care pathway and 58.3% refer KS CYP to andrology clinic. Our survey has highlighted variation in the care provided to CYP with KS. Is a UK consensus guideline for managing KS CYP warranted?

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OC5.5

Pre-hypertension genes in the avon longitudinal study of parents and children (ALSPAC) predict higher systolic blood pressure in children from the manchester babyGRO study

Reena Perchard[1,2], Lucy Higgins[1,2], Adam Stevens[1], Terence Garner[1], Philip Murray[1,2], Amirul Roslan[1], Andrew Whatmore[1], Edward Johnstone[1,2] & Peter Clayton[1,2]
[1]University of Manchester, Manchester, United Kingdom. [2]Manchester University NHS Foundation Trust, Manchester, United Kingdom

Background
Cardiometabolic risk is linked to being small for gestational age (SGA, birthweight <-2SDS). Using data from the Avon Longitudinal Study of Parents and Children (ALSPAC), an 'omic signature in SGA catch-up children predicts pre-hypertension in adolescence. Suboptimal fetal growth (SFG) alone may be linked with greater cardiometabolic risk. Therefore, we focused on cardiometabolic risk in children born following pregnancies at higher risk for SFG, irrespective of birthweight.
Aim
To validate the predictive ability of an ALSPAC-derived 'omic signature for pre-hypertension, in a Manchester cohort of children whose mothers had displayed higher risk of SFG in pregnancy.
Methods
We recruited 81 children aged 3-6 years, following term pregnancies at increased risk of SFG based on adverse maternal antenatal serology (e.g. low pregnancy associated plasma protein-A). 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. Fasting blood samples for cardiometabolic markers and transcriptomic (gene expression) analyses were collected ($n=31$). Δfetalwt ([birthweight centile minus 23-week estimated fetal weight centile]/days) and Δchildwt ([child weight centile minus birthweight centile]/years) were divided into quartiles and differences in cardiometabolic markers compared. Random forest was used to determine the predictive ability of the ALSPAC-derived 'omic signature for Q4 childhood BP in the BabyGRO cohort.
Results
69% (56/81) had Δfetalwt <0, but only 12% (10/81) were born SGA. SBP was higher and HDL lower in Δfetal Q1 (lowest intrauterine weight gain) vs Q4 ($P<0.05$). SBP, BMI SDS, AC, MUAC, AI and %fat were higher in Δchildwt Q4 (highest childhood weight gain) vs Q1 ($P<0.05$). Transcriptomic data were available for expression of 33 of 47 ALSPAC genes predictive of pre-hypertension. Random forest accurately predicted child SBP Q4 from Q1-3 (out of bag AUC 0.98, error rate 3.9%).
Conclusion
Pre-hypertension gene expression demonstrated in SGA children with catch-up growth predicts higher SBP within this cohort enriched for SFG, but where only a minority were SGA-born. This 'omic signature could aid early identification of non-SGA infants with prehypertension risk, who may require BP monitoring from early-life onwards.

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OC5.6

Can clinical, biochemical and genetic parameters help distinguish congenital hypogonadotrophic hypogonadism from self-limited delayed puberty?

Francesco d'Aniello[1,2,3], Yuri Aung[2,4], Vasilis Kokotsis[2] & Sasha R Howard[2,4]
[1]University Department, Bambino Gesù Children's Hospital, Rome, Italy. [2]Centre for Endocrinology, William Harvey Research Institute, QMUL, London, United Kingdom. [3]"Tor Vergata" University, Medicine Faculty, Rome, Italy. [4]Department of Paediatric Endocrinology, Royal London Children's Hospital, Barts Health NHS Trust, London, United Kingdom

Delayed puberty (DP) is defined as pubertal onset 2-2.5 SDs later than the general population. The most common aetiology is self-limited DP (SLDP). However, during adolescence, it is a clinical challenge to differentiate SLDP from the more severe disease congenital hypogonadotrophic hypogonadism (HH). This study sought to elucidate phenotypic and genotypic discrepancies between the two diagnoses to improve diagnosis and management. This was a retrospective study of a UK DP cohort managed from 2015-2023, identified through the NIHR clinical research network. Patients were diagnosed with SLDP if they attained Tanner stage G4/B4 by 18yrs, whereas with HH if they had not commenced (complete, cHH) or had arrested puberty (partial, pHH) before 18yrs. Auxology, Tanner staging, biochemistry, bone age, and hormonal treatment were analysed. Genetic scores, ranging from 1-5, were assigned after whole-exome sequencing and identification of predicted pathogenic variants in genes associated with either SLDP or HH (1=known SLDP variant, 2=likely SLDP variant, 3=no or overlap variant, 4=likely HH variant, 5=known HH variant). Statistical analysis was completed using IBM SPSS and R. 78 patients were included in this study. 52 (66.7%) patients had SLDP and 26 (33.3%) had HH, of whom 17 (65.4%) pHH and 9 (34.6%) cHH. Probands were predominantly male (90.4%). Male SLDP patients showed significantly lower height and weight SD at presentation ($P=0.004$, $P=0.021$). HH patients had lower testicular volumes, particularly cHH patients ($P=0.019$). 73.1% of patients with SLDP and 43.3% with HH had a family history of DP ($P=0.007$). 15.4% of SLDP, compared to 38.5% of HH patients, had classical associated features of HH (micropenis, cryptorchidism, anosmia, etc. $P=0.023$). Mean first recorded LH and inhibin B were lower in males with HH, particularly in cHH patients ($P=0.01$, $P=0.001$), but were not discriminatory due to overlapping ranges. Genetic score of SLDP patients was lower than HH patients (3.00 ± 0.55 vs 3.47 ± 0.70; $P=0.008$). Key clinical markers of auxology, associated signs, and serum inhibin B may help distinguish between SLDP and HH. These could be incorporated into a scoring system with genetic analysis to aid clinician's decision-making process. However, the distinction between partial HH and SLDP remains problematic.

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OC5.7

Breast milk-induced hypercalcaemia – a retrospective study to describe biochemical and radiological outcomes if no intervention is offered

Dr. Sandhya Govindarajan[1], Dr. Amish Chinoy[2], Dr. Imran Zamir[3], Dr. Raja Padidela[4] & Dr. Zulf Mughal[5]
[1]North Manchester General Hospital, Manchester Foundation Trust, Manchester, United Kingdom. [2]Consultant Paediatric Endocrinology, Royal Manchester Children's Hopsital, Manchester, United Kingdom. [3]Consultant Paediatrician, North Manchester General Hospital., Manchester, United Kingdom. [4]Consultant Paediatric Endocrinology, Royal Manchester Children's Hospital, Manchester, United Kingdom. [5]Consultant in Paediatric Metabolic Bone Disorders, Royal Manchester Children's Hospital, Manchester, United Kingdom

Introduction
Asymptomatic hypercalcaemia in infants who are exclusively breast-fed is recognised in clinical practice but has never been evaluated and outcomes described if breast feeding is continued.
Objective
We conducted a novel retrospective analysis to evaluate the biochemical and radiological outcomes of breast milk-induced hypercalcaemia.
Methods
A multi-site retrospective study was conducted across a 4 year period in infants noted to be hypercalcaemic (serum corrected Calcium (CCa) $\geq$2.8 mmol/L) who were exclusively breast-fed and did not have other medical conditions causing hypercalcaemia. Clinical, biochemical and radiological parameters were collected and analysed.
Results
18 infants (10 males, 8 females) were included in the analysis. Mean peak serum corrected calcium was noted to be 3.1 mmol/L (normal range 2.2-2.8 mmol/L;

standard deviation 0.2). All infants were exclusively breastfed during the detection of hypercalcaemia and were clinically asymptomatic. None of them had interventions such as locasol, intravenous fluids, diuretics or bisphosphonates. Mean serum PTH level was 0.9 pmol/L (low; reference 2.0 – 9.4 pmol/L); mean serum Vitamin D was 60.8 nmol/mL (normal; reference >50nmol/L); and mean serum phosphate level was 1.7 mmol/L (normal; reference: 1.3 – 2.6mmol/L). There was no significant correlation of peak serum cCa with corresponding PTH, phosphate and Vitamin D levels and no significant correlation between age of resolution of peak CCa and duration of breast feeding ($P<0.05$). All 18 infants had renal ultrasound, and all of them had no evidence of nephrocalcinosis on ultrasound. Mean duration of resolution of hypercalcaemia was 123 days with a range of 10 days to 329 days. Mean duration of exclusive breastfeeding was 108 days.

Conclusion

Breast milk-induced hypercalcaemia is characterised by PTH-independent hypercalcaemia. Unlike other causes of PTH-independent neonatal hypercalcaemia, it is an asymptomatic condition with no nephrocalcinosis. In view of its comparative benign clinical course, such infants with asymptomatic hypercalcaemia and absence of nephrocalcinosis can safely continue to breast feed rather than switching to low calcium formulas, which would result in loss of the many benefits of breast milk. The cause for hypercalcaemia in these infants is not yet established and would require further research.

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OC5.8

Liraglutide improves metabolic profile, glycaemic dysregulation, quality-of-life and eating behaviours in adolescents with severe obesity

Louise Apperley, Jennifer Parkinson & Senthil Senniappan
Alder Hey Children's Hospital, Liverpool, United Kingdom

Introduction

Childhood obesity is associated with various complications and medical treatment options are limited. Liraglutide, a GLP-1 receptor agonist, has shown improvement in body mass index (BMI) in clinical trials and has been licensed for clinical use in adolescents >12 years of age. The aim of our study is to evaluate the effect of liraglutide treatment on cardiometabolic variables, quality-of-life (QoL) and satiety levels in adolescents with severe obesity. To our knowledge, this is the first study reporting the use of continuous glucose monitoring (CGM) to assess the treatment effects on glycaemic variation in obesity.

Methods

24 patients aged 12-17.9 years with severe obesity completed a 3-month course of subcutaneous liraglutide treatment (maximum dose 3mg daily), along with multidisciplinary support in a tier-3 weight management service. Clinical measurements, body composition, biochemical profile and questionnaires (PedsQL 4.0 generic scale and Three-factor Eating Questionnaire R18) were collected, along with CGM insertion (blinded Dexcom G6 devices), at baseline and 3-months.

Results

Significant improvements were shown in weight [-2.95kg, $P=0.001$], BMI [-1.38kg/m2; $P<0.001$], BMI standard deviation scores [-0.09; $P=0.003$], percentage body fat [-2.09%; $P=0.043$] and fat mass [-4.00kg; $P=0.011$] following liraglutide treatment. Significant reductions in HbA1c (-1.35mmol/-mol; $P=0.025$), triglycerides (-0.122mmol/L; $P=0.010$) and cholesterol (-0.28mmol/L; $P=0.029$) were also observed. CGM revealed a significant increase in the percentage time of glucose levels within the normal range (3.9-7.8mmol/L) from 91.76 to 94.18% [$Z=-1.98$; $P=0.048$]. The percentage time spent over 10mmol/L reduced from 0.08 to 0.02% [$Z=-1.50$; $P=0.133$]. The QoL total scores were noted to improve in parent and child-reported questionnaires. Uncontrolled eating behaviours reduced significantly ($P=0.006$) and improvements in cognitive restraint and emotional eating were observed.

Conclusion

Liraglutide treatment has shown significant improvement in metabolic parameters, along with improved satiety levels and QoL. CGM has highlighted the evidence of glycaemic dysregulation in adolescents with obesity, compared to peers without diabetes or obesity, and its significant improvement following liraglutide treatment. Liraglutide could be an important treatment option for young people with severe obesity to improve physical health, eating behaviours and QoL, and CGM could be a useful tool to assess glycaemic dysregulation in adolescents with severe obesity.

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OC5.9

Home waking salivary cortisone to screen for adrenal insufficiency in children

Mathilde Tavernier[1], Callum Ross[1], Craig Jessica[1], Chamila Balagamage[2], Brian Keevil[3], Richard Ross[1], Miguel Debono[4] & Charlotte Elder[1,5]
[1]University of Sheffield, Sheffield, United Kingdom. [2]Birmingham Children's Hospital, Birmingham, United Kingdom. [3]Manchester University NHS Foundation Trust, Manchester, United Kingdom. [4]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom. [5]Sheffield Children's NHS Foundation Trust, Sheffield, United Kingdom

Background

The current screening test for adrenal insufficiency (AI) involves patients attending hospital for an "early" morning serum cortisol sample, generally taken some considerable time after the child has woken. This risks missing the morning cortisol peak, leading to false positive results. It requires venepuncture, which is unpleasant for children. Saliva collection is non-invasive, simple and can be undertaken on waking at home, providing a more physiological assessment. Home waking salivary cortisone has proven an accurate screening test for AI in adults (1), and we have investigated its use in children.

Methods

A prospective diagnostic accuracy study was performed in children attending Sheffield Children's Hospital for a Short Synacthen Test (SST). Patients collected a waking salivary sample at home on the morning of their SST. Salivary cortisol (SalF) and salivary cortisone (SalE) were measured by liquid chromatography-tandem mass spectrometry. Area under Receiver-operator characteristic (AuROC) curves were computed, and cut-off accuracies derived. Patient and carer acceptability were investigated using questionnaires.

Results

Seventy-eight patients have completed the study to date, 68 with adequate samples for analysis. Mean age was 10.6 years (SD 3.4, range 3-17 years), 52% female and 60% taking steroid medication. The prevalence of AI (defined as a peak serum cortisol post 145 mg/m2 Synacthen of <430nmol/L) was 19% ($n=13$). Waking salivary glucocorticoids predicted SST outcome with an AuROC of 0.76 (95% CI 0.60-0.92, $P=0.004$) for SalF and 0.83 (95% CI 0.73-0.93, $P=0.000$) for SalE. A waking SalE cut-off of >13.9nmol/L excluded AI with a sensitivity of 92% and a negative predictive value of 97% and would have avoided 35 (45%) SSTs. The home test was acceptable to 97%, with 86% preferring the salivary test over the SST.

Conclusions

Our data indicate that waking salivary cortisone provides an accurate, acceptable and more convenient screening test for AI. Paediatric cut-offs may be different to those recently reported in adults (1). Home waking salivary cortisone has the potential to shorten the AI diagnostic pathway, reduce false positive screen results, enabling more tailored SST diagnostic testing. Further work is needed to support implementation throughout the NHS.

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Oral Communications 6

OC6.1

An audit on improving the endocrine management of patients with Duchenne Muscular Dystrophy

Martha McKenna, Kim Stevenson, Emma Campbell, Isobel Douglas, Karen Thompson, Noina Abid & Sandya Tirupathi
Royal Belfast Hospital for Sick Children, Belfast, United Kingdom

Introduction

Duchenne Muscular Dystrophy (DMD) is an X-linked recessive neuromuscular disorder causing progressive muscular degeneration and weakness. The survival of patients with DMD has improved with multi-disciplinary team input. Subspecialties have moved towards anticipatory diagnostic and therapeutic strategies which focus on prevention and treatment of modifiable disease complications. Endocrine complications of DMD include impaired growth, delayed puberty, adrenal insufficiency and low bone mineral density (BMD).

Methods

A retrospective review of all patients with DMD in the Belfast Trust was undertaken by reviewing patient records and comparing with the NorthStar recommendations. We reviewed if patients had steroid emergency plan and if a pubertal assessment had taken place. Bone health was assessed by regular vitamin D monitoring and supplementation, surveillance imaging and appropriate treatment of low BMD. A series of actions were made based on 2021 audit findings. This included a standardised referral letter to endocrinology for surveillance of puberty and bone health at 10 years of age. An information letter

was produced for patients and parents to educate on adrenal insufficiency with an action plan for sick day rules and training for IM hydrocortisone administration. Re-audit was undertaken in 2023 to assess progress

Results

	Audit 2021	2023
Number of patients	45	44
Age range (years)	5-17	2-18
Steroids use N(%)	40/45(89%)	37/44(84%)
Steroid emergency plan/ IM hydrocortisone training N(%)	2/40(5%)	34/37(92%)
Vitamin D N(%)	41/45(91%)	41/44(93%)
Prescription	11/45(24%)	35/44(80%)
Regularly monitored	26/45(58%)	40/44(91%)
Up to date surveillance imaging N(%)	0/45(0%)	37/44(84%)
DEXA	5/45(11%)	13/44(30%)
Lateral spine x-ray	4/45(9%)	13/44(30%)
Compression fracture N(%)		
Zolendronic acid treatment N(%)		
Endocrine referral >10 years of age	4/39(10%)	34/38(89%)
Pubertal assessment N(%)*	3/4(75%)	34/34(100%)
Treatment for delayed puberty N(%)*	2/4(50%)	11/34(32%)

*Undertaken in patients referred to the endocrine team

Conclusion

An improvement has been demonstrated in the management of endocrine complications associated with DMD but there are still areas which require further work. Ongoing multi-disciplinary input and partnership is required to optimise management for patients with DMD.

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OC6.2

Children with hypophosphatasia treated with asfotase alfa: analysis from the UK Patients Cohort

Raja Padidela[1], Nick Bishop[2,3], Paul Arundel[2], Shona Fang[4], Alexandros Zygouras[4], Zulf Mughal[1], Nick Shaw[5] & Vrinda Saraff[5]
[1]Manchester Children's Hospital, Manchester, United Kingdom. [2]Sheffield Children's Hospital, Sheffield, United Kingdom. [3]University of Sheffield, Sheffield, United Kingdom. [4]Alexion, AstraZeneca Rare Disease, Boston, USA. [5]Birmingham Women's and Children's Hospital, Birmingham, United Kingdom

Objective

To describe outcomes among children with hypophosphatasia (HPP) receiving asfotase alfa.

Methods

This prospective, real-world study used data from all children with HPP receiving asfotase alfa in the UK Managed Access Agreement (MAA) to assess functional, health-related quality-of-life, and safety outcomes. Visits occurred at MAA enrolment, 3 and 6 months after enrolment, and every 6 months thereafter. Assessments at visits were age appropriate: Brief Assessment of Motor Function (BAMF), 1–4 years; Pediatric Quality of Life Inventory (PedsQL), 2–18 years for parent-reported and 5–18 years for child-reported; and modified Bleck and 6-Minute Walk Test (6MWT), 5–18 years. Values, including at first assessment, are presented as median (min, max; n); outcomes from first assessment to 48 months (BAMF: 36 months) are presented as median change (95%CI; n).

Results

All 24 children enrolled received $\geq$1 asfotase alfa dose; the study population comprised 20 with $\geq$6 months' exposure (9 male [45%]; 12 initiating asfotase alfa pre-MAA enrolment [60%]). Age at enrolment was 4.17 (0, 17) years; asfotase alfa treatment duration before enrolment was 3.67 (0.53, 10.10) years. Height Z-score at first assessment was -2.42 (-9.53, -0.28; $n=20$) and changed by 0.34 (95%CI: -0.34, 1.35; $n=12$); weight Z-score was -1.86 (-4.93, 1.43; $n=20$) and changed by 0.20 (95%CI: -1.06, 0.98; $n=12$). BAMF scores for lower extremities (LEs) and upper extremities (UEs) were 6 (0, 10; $n=7$) and 9 (0, 9; $n=7$), respectively, and improved for LEs (7 [95%CI: 3.19, 11.84]; $n=3$) and UEs (7 [95%CI: 3.19, 11.84]; $n=3$). Parent- and child-reported PedsQL scores were 53.42 (16.30, 100.00; $n=18$) and 59.24 (15.22, 91.30; $n=10$), respectively, and improved by 12.97 (95%CI: 1.94, 24.56; $n=10$) and 13.04 (95%CI: -4.81, 30.04; $n=6$), respectively. Starting Bleck scores were relatively high (9 [5, 9]; $n=14$) and remained stable (0 [95%CI: -1.19, 1.32]; $n=6$). The 6MWT percent predicted values started at 57.89 (12.41, 90.72; $n=11$) and changed by 3.28 (95%CI: -26.15, 34.13; $n=4$). Serious adverse events were infrequent ($n=9$, 16 events), with 1 event (injection site atrophy) related to asfotase alfa.

Conclusion

Asfotase alfa treatment helped children with HPP in the UK MAA maintain stable outcomes.

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OC6.3

Initial experiences of using the Paediatric Sleep Questionnaire (PSQ) to screen for obstructive sleep apnoea in a tier-3 paediatric weight management clinic

Katherine Hawton[1,2], Juliette Oakley[1], Simon C Langton-Hewer[1,2], Tasmin Sharley[1], Dinesh Giri[1,2] & Julian Hamilton-Shield[3,1]
[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom. [2]University of Bristol, Bristol, United Kingdom. [3]NIHR Biomedical Research Centre (Nutrition), University of Bristol, Bristol, United Kingdom

Background

Obstructive sleep apnoea (OSA) is characterised by recurrent upper airway obstruction during sleep resulting in abnormal ventilation and sleep patterns. Paediatric obesity is associated with a significantly increased OSA risk. Prompt recognition and management of OSA is important to reduce the risk of complications, including cardiovascular, growth, behavioural and glycaemic. We describe initial experiences of using the Paediatric Sleep Questionnaire (PSQ) to screen for OSA in severe paediatric obesity.

Method

71 new patients seen in a tier-3 paediatric weight management clinic had a history taken and a PSQ performed. The PSQ is a 22-question validated screening tool, with 0.33 and 0.66 having previously been identified as cut-offs for likely mild and moderate/severe OSA respectively. Patients with a score of $\geq$ 0.33 and/or a history suggestive of OSA were referred to a tertiary paediatric respiratory team for further investigation using an oximetry study and/or cardiorespiratory sleep study (CrSS).

Results

Patients (38 male, 33 female) aged between 3.3-17.0 years (mean 12.0) with mean BMI-SDS 3.41(1.68-5.93). Mean PSQ score (table 1) was 0.48(0.05-0.91) and 59.2% patients were referred for respiratory assessment. 13 sleep studies have been completed (6 oximetry, 7 CrSS). 6/13(46.2%) were diagnosed with OSA requiring non-invasive ventilation and a further 3/13(23.1%) patients had borderline oximetry studies and are awaiting a formal CrSS.

Table 1. PSQ scores and outcomes:

PSQ score	N	History suggestive of OSA	Referred to respiratory team	Sleep studies completed	Results of sleep study		
					OSA	No	Borderline
< 0.33	20 (28.2%)	0 (0%)	0 (0%)	0	0	0	0
≥ 0.33 but < 0.66	33 (46.5%)	22 (66.7%)	24 (72.7%)	5	2	2	1
≥ 0.66	18 (25.4%)	18 (100%)	18 (100%)	8	4	2	2

Conclusions

Our preliminary data demonstrate that our weight management service is effectively screening for OSA, with several patients commencing NIV as a result of attending since questionnaire implementation. PSQ scores align with histories suggestive of OSA in this population and may assist with triaging for sleep studies. There is a paucity of evidence regarding effective screening for OSA in severe paediatric obesity and further work in this area is warranted.

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OC6.4

Screening for coeliac disease in paediatric patients diagnosed with Graves' Disease

Owen Bendor-Samuel & Taffy Makaya
Oxford Children's Hospital, Oxford, United Kingdom

Introduction

Our current local management guidelines for Graves' Disease (GD) in children and young people (CYP) do not include routine screening for coeliac disease (CD). However, ad hoc testing of patients in this cohort pointed to a high incidence of positive tissue transglutaminase (TTG) results.

Aims/Objectives

1. To determine the incidence of CD in patients in our service diagnosed with GD.
2. To establish if a review of our GD management guideline was needed.

Methods
We reviewed the results of all patients aged 0-17 years in our service diagnosed with GD (TSH-receptor antibody positive, with biochemical thyrotoxicosis) between 01/01/2010-31/12/2022 - 13 years inclusive. We undertook a review of the literature in this field.
Results
$n=41$ patients fulfilled the inclusion criteria and had a full data set. 78% were female, and the age range was 3-17 years, with a mode and median of 12-15years ($n=23$). The peak incidence of GD diagnosis was 2020 and 2021 (7 per each year), which coincided with the COVID-19 pandemic.
Coeliac serology:
54% of our patients with GD ($n=22/41$) had been tested for coeliac (TTG-analysis). Of these, 23% ($n=5/22$) were positive and diagnosed with CD.
Discussion
The general population incidence of CD is about 1%. A 2016 meta-analysis of the prevalence of CD in autoimmune thyroid disease (Hashimoto's and Graves') showed an overall incidence of 6.2% in CYP. In a further study looking specifically at coeliac disease in CYP with Graves' disease, Larizza *et al*., found the incidence was 4.6% ($n=1/22$). A review of current guidelines in this field showed that the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) guidelines for the diagnosis of CD advocate screening in patients with GD; and an Italian paper by Beteerle *et al*. suggests screening at diagnosis and every 2-3 years if negative.
Conclusion
Based on the findings from our review, which confirm the high incidence of CD in CYP with GD, and in line with the ESPGHAN guidelines, we have now modified our management guidelines to include screening for CD in all CYP with GD, at diagnosis and ever 2-3 years thereafter.

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OC6.5

Growth hormone excess in children with pituitary adenomas associated with endocrine syndromes

Julie Park[1], Christina Daousi[2,3] & Joanne Blair[1]
[1]Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom. [2]The Walton Centre, Liverpool, United Kingdom. [3]Aintree University Hospital, Liverpool, United Kingdom

Growth hormone (GH) excess is extremely rare in children. It can be associated with endocrine syndromes including MEN1, Carney complex and Mc Cune Albright syndrome. We describe two cases of GH excess and their management. Patient A (15yr M) presented with fibrous dysplasia affecting his cranium and a large café-au-lait spot covering his right scapula. His height was 193cm (2.6 SDS) and BMI 29.6kg/m2(2.3SDS). His IGF1 was 84.1nmol/L (22.5 – 65.9) and GH did not suppress during an oral glucose tolerance test (OGTT) (GH nadir 1.43ug/L). Skeletal survey showed no other bony lesions. MRI of the pituitary was normal. Ophthalmology showed no effect on optic nerve or visual fields. Patient B (15M) had an antenatal diagnosis of a PRKAR1A gene change consistent with Carney Complex. Puberty commenced aged 10 years. Height SDS increased from 1SDS to 2.8SDS. GH did not suppress on OGTT (GH nadir 3.18ug/L), and IGF-I was 55.9nmol/L. Both children were discussed within the Merseyside pituitary MDT and with colleagues nationally. Treatment options including watchful wait, somatostatin analogues, GH antagonists, radiotherapy and pituitary surgery were discussed. Both patients commenced treatment with Lanreotide®, a somatostatin analogue. Patient A commenced medical therapy immediately as it has been reported that growth of fibrous dysplasia lesions slow or stop. However, shrinkage is not described. His IGF1 reduced from 131nmol/L to 96nmol/L after commencing treatment. Patient B initially underwent a period of observation. However, the pituitary adenoma increased in size (baseline 9x13x7mm vs 14x18x15mm) and medical therapy was commenced. After six months, the adenoma measured 10x14x6mm, IGF1 concentrations and height velocity have plateaued. His HbA1c is 43 mmol/mol/L (20 – 42 mmol/mol). Both patients tolerated treatment well. GH secreting tumours are rare in childhood. It has been described that somatostatin analogues may cause tumour shrinkage but are not always associated with a fall in IGF1. Patient B may still require further treatment. GH antagonists are rarely used in children and little data are available regarding their use. Pituitary surgery comes with possible life changing complications and multiple pituitary hormone deficiencies. Remission rate is not 100%.

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Oral Communications 7

OC7.1

Integrating physical activity in structured education programmes to lower hyperglycaemia in children and young people with type 1 diabetes without increasing risk of hypoglycaemia

John Stuart Pemberton[1], Gar Mun Lau[2,3], Ankita Gupta[2], India Dickinson[2], Pranav Viswanath Iver[2] & Suma Uday[1,4]
[1]Department of Endocrinology and Diabetes, Birmingham Children's Hospital, Birmingham, United Kingdom. [2]University of Birmingham, Birmingham, United Kingdom. [3]Walsall Manor Hospital, Walsall, United Kingdom. [4]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom

Objectives
Investigate the effect of using moderate intensity activity between meals to lower hyperglycaemia on glucose metrics in children and young people with type 1 diabetes (CYPD).
Design & Methods
Retrospective data from CYPD attending a continuous glucose monitoring (CGM) education programme at a tertiary centre between 2019 and 2022 were analysed. CYPD were taught to use moderate intensity activity to lower hyperglycaemia between meals (to less than 10.0 mmol/L by using 10-15 minutes for every 2 mmol/L). CYPD >5 years with minimum 6 month data and at least 70% CGM data capture were included. CYPD <2 years from diagnosis were excluded due to honeymoon effect. Data were collected on demographics and baseline and six months glucose metrics [Hba1c, time in range (TIR, 3.9-10.0 mmol/L), time above range (TAR, >10.0 mmol/L), time below range (TBR, <3.9 mmol/L), TAR2 (>13.9 mmol/L)]. At six months, information on minutes of activity used to lower glucose level $>$ 14.0 mmol/L trending steady was gathered through a self-reported questionnaire. CYPD were grouped into low (<5 minutes), mild (5-10 minutes), or moderate (11-20 minutes) activity groups.
Results
125 ($n=$ 53, 40% male) CYPD with a mean (SD) age of 12.3 ($\pm$3.7) years and diabetes duration of 7.0 ($\pm$3.7) years were included. Baseline HbA1c was 58.5 ($\pm$ 8.7) mmol/mol. Low, mild and moderate activity was reported by 30% ($n=37$), 34% ($n=43$) and 36% ($n=45$) respectively. At 6-months, HbA1c (52.0 vs. 54.3 vs. 59.4 mmol/mol, $P<0.001$), TIR (68.0% vs. 59.71 vs. 51.1%, $P<0.001$), TAR (29.9% vs. 38.3% vs. 45.3%, $P<0.001$) and TAR2 (7.6% vs.11.0% vs. 16.1%, $P<0.001$) were significantly different across the moderate, mild, and low activity groups, respectively. No differences were found for TBR (2.16% vs. 2.32% vs. 2.58%, $P=0.408$) across groups. CYPD in the low activity group were younger, predominantly females, and from the most deprived socioeconomic quintile. Moderate intensity activity is more likely to be used by males and older age groups.
Conclusion
Moderate intensity activity to lower hyperglycaemia between meals improves glycaemic control without increasing risk of hypoglycaemia in CYPD. Socio-economic barriers to implementation need further exploring.

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OC7.2

Retrospective audit of the East of England, Children and Young People Diabetes Network, out of hours consortium provision

Ruth Francks
Mid and South Essex NHS Trust, Basildon, United Kingdom

Introduction
In 2011, the East of England Children and Young Peoples Diabetes Network (EECYPN) sought to find a solution to the provision of out of hours advice regionally, and coordinated the development of the Out of Hours (OoH) Consortium.
Objectives
- To review the timing, nature and outcome of the calls received to the Out of Hours service over a 12-month period (1 April 2021 and 31 March 2022).
- To highlight patterns and trends in the numbers and frequency of calls
- To identify the common themes in calls to highlight areas of improvement in education to C&YP and their families

Method
Each call to the Out of Hour's consortium is documented on the 'Out of Hours Contact Form'. All call details were logged on the data capture sheet and returned to the author for collation and analysis.
Summary of Results
1) In excess of 661 calls were made to the Out of Hours service between 1 April 2021 and 31 March 2022. 2) Advice on management of hyperglycaemia, equipment

problems and sick day advice were the most common reasons for calling 3)The months of February, July, September had the the least number of calls. 4) Most calls are received between the hours of 17:00 -24:00 (63.4%).5) The average length of each call was 10 minutes. 6) Most of the contact with the OOH service was from the mums of our children and young people (77%), 7) A symmetrical distribution of calls by age 8) An overwhelming 86% of calls were managed at home and avoided possible hospital attendance 9) 11% of callers were advised to attend their local A&E department

Conclusions

The audit has demonstrated that the EECYPDN Out of Hours Consortium is well utilised by CYP and their families across the region. Calls to the service are largely appropriate and 86% of the problems were resolved by the clinical on-call team

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OC7.3

Title: How do Accident and Emergency staff perceive new diabetes technologies? A study across two centers

Vasiliki Alexopoulou[1], Liana McCaffrey[1], Miranda Mccabe[1] & Sze May Ng[1,2,3]

[1]Paediatric Department, Southport and Ormskirk NHS Trust, Ormskirk, United Kingdom. [2]Department of Women's and Children's Health, University of Liverpool, Liverpool, United Kingdom. [3]Faculty of Health, Social Care & Medicine, Edge Hill University, Ormskirk, United Kingdom

Objectives

The use of new diabetes technologies, such as insulin pumps, continuous glucose monitoring systems (CGMs) and hybrid closed-loop systems (HCL), is rapidly increasing among people with type 1 diabetes (T1DM). As these technologies are becoming an integral part of T1DM management, we expect an increase in the number of patients who present in the Accident and Emergency department (A&E) using them. The aim of this study was to assess and compare A&E doctors' and Advanced Nurse Practitioners' (ANPs) knowledge, skills, perceptions and behaviors around new diabetes technologies in a tertiary and in a district general hospital (DGH) A&E department.

Methods

This was a mixed methods study. Quantitative data were collected using a 5 point Likert scale validated survey. Qualitative data were collected through semi structured interviews with a focus group of 16 doctors.

Results

In the quantitative arm of the study, 56 participants reported limited understanding of insulin pumps and CGMs and low confidence when managing patients on these devices. Understanding of diabetes devices was perceived as very important by A&E staff, but the education around them has been limited. No significant differences were noted in responses between tertiary and DGH participants. (Table 1) In the qualitative part of the study, low confidence was reported by 94% of doctors when managing patients on diabetes technologies. Fear and anxiety were also common feelings. All doctors agreed that more training on the new diabetes technologies would be very important to improve their confidence and patient experience.

Conclusions

Formal education of A&E staff around new diabetes technologies appeared essential and could improve the quality of care provided to patients with T1DM presenting to A&E.

Table 1. Survey main results (means of 5 point scale).

	Tertiary Hospital	DGH
Appropriate understanding of pumps/CGMs	2.1 / 2.0	2.6 / 1.9
Could appropriately manage a patient on a pump / CGM	2.3 / 2.1	2.3 / 2.1
Importance of understanding of pumps / CGMs in A&E	3.8 / 3.7	4.2 / 4.1
Education received on pumps / CGMs	3.8 / 3.7	4.2 / 4.1
Education received on pumps / CGMs	2.1 / 2.2	1.9 / 2.1

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OC7.4

T1D clinic- a novel approach!

Sarinda Millar & Edel Magee
SHSCT, Newry, United Kingdom

In collaboration with local borough councils and the League of Diabetes and in response to severe staff shortages, the Southern Health & Social Care Trust (SHSCT), Northern Ireland, Type 1 Diabetes (T1D) team ran age banded group clinics at local Leisure centres. Due to unexpected and challenging staffing issues within the T1D team we had to think outside the box as to how we would deliver 'clinic' appointments in a timely manner to our children and young people in adherence with NICE guidelines.

The aim of the alternate clinic model was twofold:

- To bring our children, young people and their families together outside of the usual hospital environment affording invaluable opportunities for peer support and to meet other families living with T1D.
- To provide an educational, holistic and inspirational appointment.

The 'Diathlete', Gavin Griffiths delivered an inspirational and empowering talk at each group session. He also ran workshops with the young people. Feedback from attendees found these sessions extremely powerful and encouraging. We included short interactive sessions covering sick day rules and hypoglycaemia management. A person living with T1D has multiple appointments. To help reduce appointment burden we invited our local podiatry and regional retinal screening services. Our SHSCT psychology team provided an overview of the support they can offer on a one-one basis and via group sessions available for not only those living with T1D but also for their siblings and families. Charitable organisations provided an overview of the events/projects taking place for our children and young people living with T1D in Northern Ireland and further afield. Due to the evolving technological advances in the management of T1D we felt it imperative to include diabetes technology representatives. This allowed our service users to engage directly with the company representatives. Feedback was obtained from service users, their parents /carers and from professionals attending the sessions. This was overwhelmingly positive. It is our intention to run these age banded group sessions annually replacing 1 standard clinic appointment per year with this model. Part of the success of these sessions was giving families the opportunity to meet and share experiences.

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OC7.5

Leicester Paediatric Diabetes Unit's 'Bridge the Gap' project: Improving access to diabetes technology for children and young people from ethnic minorities and socio-economically deprived families

Manju Chandwani, Michele Collins, Farah Kazi, Laura Heath, Aan Mayes, Katy Sparrow, Megan Jeffrey, Khadija Patel & Prem Sundaram
Leicester Royal Infirmary, Leicester, United Kingdom

The National Paediatric Diabetes Audit 2021 uncovered widening disparity in the utilisation of diabetes technologies among children and young people (CYP) with type 1 diabetes from ethnic minorities and low socioeconomic groups. Our data revealed that only 27.5% of CYP from ethnic minorities were using insulin pump therapy, compared to 50% from a white background. Unfortunately, our current staffing levels and available resources were inadequate to address this issue effectively. However, we were fortunate to receive funding from the NHSE Diabetes Transformation Programme to enhance access to diabetes technologies for CYP from ethnic minorities and low socioeconomic groups. To achieve our objective, we established additional Bridge the Gap clinics during evenings and weekends and offered structured education and support to children and families both before and after adopting diabetes technologies. The funding allowed us to extend the working hours of diabetes specialist nurses and dieticians. Furthermore, we deployed a support worker proficient in the languages spoken by the families to facilitate communication and provide essential assistance during clinic sessions. Between October 2022 and March 2023, we successfully initiated 14 CYP on insulin pumps, including 11 from ethnic minorities and 3 from low socioeconomic backgrounds. Among the families, only 2 spoke English as their first language, while the others communicated in South Asian, Somalian, African, and Albanian languages. The average age at pump initiation was 10.7 years (range 4.2 to 16.1). Out of the 14 children, 13 are using Libre 2, and 1 child is using Dexcom G6. Prior to starting pump therapy, the average HbA1c level for this group was 74.1 mmol/mol (range 54 to 112). Three months after initiating pump therapy, their average HbA1c level reduced to 67 mmol/mol (range 50 to 90). During our interventions, we identified key barriers to accessing diabetes technologies. These included attempts to conceal the diagnosis due to associated stigma, limited numeracy and IT skills among caregivers, and a lack of culturally appropriate resources for learning and managing food items. Overcoming these obstacles will be crucial in ensuring improved access to diabetes-related technologies for CYP from ethnic minorities and lower socioeconomic groups.

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Oral Communications 8

OC8.1

Is there reversal of virilisation after commencing medical replacement therapy for 46XX classical congenital adrenal hyperplasia (CAH)?

Supul Hennayake, Anju Goyal & Leena Patel
Royal Manchester Children's Hospital, Manchester, United Kingdom

Genitalia appear larger and swollen in all neonates due to the circulating maternal hormones and this subsides spontaneously over few weeks or months. Additionally, general growth of the rest of the body outpaces any growth of the genitalia during childhood, resulting in apparent reduction in the size of the genitalia comparatively. There are high levels of circulating androgens in children with CAH until the commencement of medical replacement therapy (MRT). It is universally believed that the clitoris becomes smaller and virilisation reverses to some degree after starting MRT for CAH. Our aim was to assess changes in the clitoral length and virilisation parameters objectively.

Methods

Urogenital anatomy was prospectively studied in all consecutive 46XX CAH subjects by the first author from January 2003 to June 2023. The appearance of genitalia were described, and the stretched length of the clitoris was measured by the attending surgeon at the neonatal assessment. Subsequently, lengths of clitoris, common channel (CC), vagina and urethra were measured at an early cystoscopic assessment and later during feminising genitoplasty.

Results.

38 patients had surgery during this period: 18% were Prader 5 and 76% were Prader 3 or 4. Eleven patients were excluded as they did not have cystoscopic assessments. There was no reduction in clitoral length or common channel length at any stage.

$n=27$	Neonatal assessment	At cystoscopy at median age of 10 months (range 3m-17m)	At genitoplasty at median age of 20 months (range 4m-16 years)
Mean Clitoral length in mm (SD)	17.15 (5.65)	19.4 (6.22)	28 (10.31)
Mean Common Channel length in mm (SD)		20 (6.14)	25.8 (8.08)

Conclusion

Due to widely held belief regarding improvement in the appearance of genitalia after MRT, decision for genitoplasty is deferred till the extent of improvement is clear. However, serial assessment of clitoral and common channel lengths failed to show any actual reduction in size.

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OC8.2

Rare variants in the MECP2 gene in girls with central precocious puberty

Jordan Read[1], Leonardo Guasti[1], Alyssa Paganoni[1] & Sasha Howard[1,2]
[1]Queen Mary University of London, London, United Kingdom. [2]Barts Health NHS Trust, London, United Kingdom

Key genetic contributors are recognised to underlie the phenotype of central precocious puberty (CPP), including the imprinted genes Makorin ring finger protein 3 (MKRN3) and Delta-like homolog 1 (DLK1), alongside Kisspeptin-1 (KISS1) and (KISSR1). These genes have implicated mis-regulation of transcriptional control of the kisspeptin and gonadotropin-releasing hormone (GnRH) neuroendocrine systems in onset of CPP. However, many familial cases of CPP remain without clear a genetic aetiology. We recently published a large cohort study identifying CPP associated variants in Methyl-CpG-binding protein 2 (MECP2), a chromatin-associated transcriptional regulator, with known roles in neuronal maturation (Canton *et al*, 2023 Lancet Diabetes and Endocrinology). MECP2 is encoded by a gene on Xq28, is highly expressed in hypothalamic nuclei and co-localises with GnRH within GnRH neurons, suggesting a role in puberty onset through regulation of the GnRH neuronal axis. Loss-of-function mutations in MECP2 are usually associated with Rett syndrome, a severe neurodevelopment disorder characterized by developmental regression and intellectual disability. Interestingly, patients with Rett syndrome loss-of-function variants in MECP2 are reported with precocious timing of puberty onset. We investigated the *in vitro* impact of 5 CPP associated and 2 Rett syndrome associated MECP2 variants in a GT1-7 mouse neuronal GnRH producing cell line. Immunocytochemistry of MECP2 variant overexpressing GT1-7 identified differential expression of CPP associated and Rett associated MECP2 variants. Western blotting confirmed differential protein expression of overexpressed MECP2 variants of interest compared to wildtype MECP2. Preliminary studies in a GnRH reporter system demonstrated differential ability of MECP2 variants to suppress GnRH promoter activity, suggesting a possible regulatory role in the GNRH neuronal network. Here we present data suggesting that CPP associated variants in MECP2 alter protein expression and localisation within a GnRH neuronal cell line. Mechanisms of action of gene regulation by MECP2 is complex, comprising transcriptional regulation and chromatin compaction, thus further studies are required to determine the molecular basis of MECP2 regulation of the GnRH neuroendocrine axis. Identification of key differences in expression and activity of CPP associated MECP2 variants, compared to those associated with Rett syndrome, can aid in genetic diagnosis and treatment of patients.

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OC8.3

Dysregulated pathways reveal NOVEL mechanistic insights underlying HMGA2-related growth failure in Silver Russell Syndrome

Avinaash Maharaj[1], Emily Cottrell[1], Ahmed Massoud[2], Vivian Hwa[3] & Helen Storr[1]
[1]Centre for Endocrinology, William Harvey Research Institute, QMUL, London, United Kingdom. [2]Department of Paediatrics and Child Health, HCA Healthcare UK, London, United Kingdom. [3]Cincinnati Center for Growth Disorders, Division of Endocrinology, Cincinnati Children's Hospital Medical Center, Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, USA

Background

Silver Russell syndrome (SRS) is a heterogeneous disorder characterised by intrauterine and post-natal growth retardation, relative macrocephaly, protruding forehead, feeding difficulties and body asymmetry. Variants in *HMGA2* are a rare cause of SRS and despite strong evidence for the crucial role of HMGA2 in growth regulation, the underlying mechanism underlying growth retardation has, thus far, not been elucidated.

Methods

Our cohort of undiagnosed patients with SRS were genotyped. A missense variant, *c.166A>G* (p.K56E) predicted to abrogate DNA-binding was created by mutagenesis of an N-terminal FLAG tagged-*HMGA2* cDNA clone. HMGA2-WT (wild type) and variant expression and nuclear localisation were assessed by immunoblotting and confocal microscopy in HEK293 cells which lack endogenous HMGA2. Markers of the integrated stress response and STAT signalling were probed by immunoblotting. Transcript levels of *IGF2* and *PLAG1* were quantified in wild-type and variant mRNA.

Results

Our cohort of six heterogeneous SRS patients with variable height SDS (range -3.2 to -3.9) and IGF-1 SDS (range from -1.9 to +4.4) were found to have deleterious variants in *HMGA2* with differing functional impacts. Microcephaly appeared to be a highly penetrant and consistent feature in these subjects highlighting the pleiotropic nature of variants in *HMGA2* since mutation type often does not predict SRS phenotypic expression. Nuclear localisation was attenuated for all variants except the well-expressed, *c.166A>G* (p.K56E), that retained functional DNA-binding AT hook domains. Transient expression of this variant in HEK293 cells was associated with downregulation of *IGF2* mRNA transcript levels when compared to *HMGA2* wild type. *PLAG1* levels were unaltered. Immunoblotting revealed significant upregulation of endoplasmic reticulum stress markers, phosphorylated STAT3 and phosphorylated eIF2α (serine 51).

Conclusion

Our data has uncovered a novel, substantial role for HMGA2 in modulating cellular chronic stress responses. Loss of functional HMGA2 leads to STAT3 hyperactivation, an event known to inhibit human growth and concomitant potentiation of eIF2α phosphorylation, a key initiator of macroautophagy. Our *in vitro* model suggests that *HMGA2* is crucial for *IGF2* transcription and its absence may potentiate macroautophagy, a response to misfolded proteins.

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OC8.4

Association of newborn screening of congenital adrenal hyperplasia with outcomes in the first 90 days of life: a multi-centre I-CAH registry analysis of contemporary practice

David BN Lim[1], Jillian Bryce[2], Salma R Ali[2,3], Xanthippi Tseretopoulou[2,3], Niels H Birkebaek[4], Sabine E Hannema[5], Ariadna Campos-Martorell[6],

Maria Clemente[6], Uta Neumann[7], Christa E Flück[8], Sara Metzger[8], Ruth E Krone[9], Alina German[10], Federico Baronio[11], Navoda Atapattu[12], Sumudu N Seneviratne[13], Martine Cools[14], Théry Mieke[14], Tulay Guran[15], Zehra Yavas Abali[15], Antony Fu[16], Dominika Janus[17], Malgorzata Wasniewska[18], Roberto Coco[18], Gianni Russo[19], Marianna Rita Stancampiano[19], Walter Bonfig[20,21], Mariacarolina Salerno[22], Hedi L Claahsen-Van Der Grinten[23], Bas P.H. Adriaansen[23], Tania Bachega[24], Mirela C Miranda[24], Otilia Marginean[25], Luisa De Sanctis[26], Ursina Probst[27], Nina Lenherr-Taube[28], Daniel Konrad[28], Michele O'Connell[29], Aneta Gawlik[30], David E Sandberg[31], Margarett Shnorhavorian[32], Nils Krone[33], S Faisal Ahmed[2,3] & Justin H Davies[1]

[1]Department of Paediatric Endocrinology, University Hospital Southampton, Southampton, United Kingdom. [2]Office for Rare Conditions, Royal Hospital for Children & Queen Elizabeth University Hospital, Glasgow, United Kingdom. [3]Developmental Endocrinology Research Group, School of Medicine, Dentistry & Nursing, University of Glasgow, Glasgow, United Kingdom. [4]Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark. [5]Department of Paediatric Endocrinology, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, Netherlands. [6]Department of Paediatric Endocrinology, Hospital Universitari Vall d'Hebron, Barcelona, Spain. [7]Clinic for Paediatric Endocrinology and Diabetes, Charité Universitätsmedizin Berlin, Berlin, Germany. [8]Paediatric Endocrinology and Diabetology, University Children's Hospital Bern, Bern, Switzerland. [9]Paediatric Endocrinology, Birmingham Women's and Children's Hospital, Birmingham, United Kingdom. [10]Paediatric Endocrinology and Diabetes, Haemek Medical Center, Afula, Israel. [11]Paediatric Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Policlinico di S. Orsola, Bologna, Italy. [12]Endocrinology, Lady Ridgeway Hospital for Children, Colombo, Sri Lanka. [13]Department of Paediatrics, Faculty of Medicine, University of Colombo, Colombo, Sri Lanka. [14]Department of Paediatric Endocrinology, Ghent University Hospital, Ghent, Belgium. [15]Department of Paediatric Endocrinology and Diabetes, Marmara University, Istanbul, Turkey. [16]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Kowloon, Hong Kong. [17]Department of Paediatric and Adolescent Endocrinology, University Children's Hospital, Jagiellonian University, Krakow, Poland. [18]Department of Human Pathology of Adulthood and Childhood, Division of Paediatrics, University of Messina, Messina, Italy. [19]Department of Paediatrics, Endocrine Unit, IRCCS San Raffaele Scientific Institute, Endo-ERN Centre for Rare Endocrine Conditions, Milan, Italy. [20]Department of Paediatrics, Technical University München, Munich, Germany. [21]Klinikum Wels-Grieskirchen, Wels, Austria. [22]Paediatric Endocrine Unit, Department of Translational Medical Sciences, University Federico II, Naples, Italy. [23]Department of Paediatric Endocrinology, Radboud University Medical Centre, Amalia Children's Hospital, Nijmegen, Netherlands. [24]Division of Endocrinology, Hospital das Clínicas, School of Medicine, University of São Paulo, São Paulo, Brazil. [25]Ist Pediatric Clinic, Research Center of Disturbances of Growth and Development in Children-BELIVE, University of Medicine and Pharmacy "Victor Babes", Timisoara, Romania. [26]Department of Paediatric Endocrinology, Regina Margherita Children's Hospital, Torino, Italy. [27]Paediatric Department, Kantonsspital Winterthur, Winterthur, Switzerland. [28]Department of Endocrinology & Diabetology, University Children's Hospital Zurich, University of Zurich, Zurich, Switzerland. [29]Department of Endocrinology, Royal Children's Hospital, Melbourne, Australia. [30]Department of Paediatrics and Paediatric Endocrinology, Medical University of Silesia, Katowice, Poland. [31]Susan B. Meister Child Health Evaluation & Research (CHEAR) Center, University of Michigan, Ann Arbor, MI, USA. [32]Division of Urology, Seattle Children's Hospital, Seattle, WA, USA. [33]Department of Oncology and Metabolism, University of Sheffield, Sheffield, United Kingdom

Aims
We studied the association of newborn screening (NBS) on early infancy outcomes in 21-hydroxylase deficiency (21OHD) congenital adrenal hyperplasia (CAH), using I-CAH registry data.
Methods
From 2018-2023, data was available for 121 infants with 21OHD CAH (52 male) during the first 90 days of life from 26 centres in 15 countries. NBS was performed in 15 centres from 9 countries.
Results
Of the 121, NBS was performed in 78 (64%) of whom 35 (45%) had CAH diagnosed prior to result notification. Diagnosis modes included: positive NBS (GrpA) (36%, males:females 33:10), atypical genitalia (GrpB) (34%, 0:41), adrenal insufficiency with/without adrenal crisis (AC) (GrpC) (17%, 14:6), prenatal diagnosis (14%, 5:12). Diagnosis by NBS was commoner in males (33/40) than females (10/38) ($P<0.0001$). Median age at presentation in GrpA (i.e. result notification) was 7d [range 2,28] vs 0d [0,19] in GrpB ($P<0.00001$) and 15.5d [4,55] in GrpC ($P<0.00001$). Median age at treatment initiation in GrpA was 9d [3,2] vs 5d [1,26] in GrpB ($P<0.001$) and 15d [7,81] in GrpC ($P<0.001$). Frequency of AC at initial presentation in GrpA and GrpB was 4/43 and 2/41 respectively ($P=0.68$). Proportion of patients with AC post-treatment was similar in GrpA, GrpB and GrpC at 4/43, 2/20 and 7/41 respectively (no significant difference). Frequency of pre-treatment hyponatraemia (27/43), hyperkalaemia (30/43) and hypoglycaemia (5/43) in GrpA was similar to GrpB (17/39, 20/38, 6/38 respectively) ($P=0.12$, $P=0.17$, $P=0.75$ respectively), but lower than GrpC (18/19, 18/19, 4/18 respectively) ($P=0.01$, $P=0.05$, $P=0.43$ respectively). At 90 days, frequency of hyponatraemia (3/38) and hyperkalaemia (8/33) in GrpA was similar to GrpB (2/28, 2/16 respectively) ($P=1$, $P=0.76$ respectively) and GrpC (2/16, 4/16 respectively) ($P=0.63$, $P=1$ respectively). Total hospitalisation duration during the first 90 days in GrpA was 10d [0,29] vs 10d [2,40] in GrpB ($P=0.23$) and 16d [2,40] in GrpC ($P=0.02$).
Conclusion
Benefits of diagnosing CAH by NBS include earlier age at diagnosis, earlier treatment initiation, reduced pre-treatment biochemical disturbance and AC, and shorter hospitalisation; these may be particularly evident in boys. However, by 90 days those diagnosed by NBS showed no differences in biochemical abnormalities and post-treatment AC frequency vs other means.

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OC8.5

Feasibility of integrating an exercise specialist supported by mHealth technology to increase exercise and physical activity in an adolescent Complications from Excess Weight Service: MOTIVATE-CEW

Andrew Davies[1], Katie Hesketh[2], Ellie Clarke[3], Louise Apperley[3], Victoria Sprung[1], Helen Jones[1], Florence Kinnafick[4], Senthil Senniappan[3] & Matthew Cocks[1]

[1]Liverpool John Moores University, Liverpool, United Kingdom. [2]Birmingham University, Birmingham, United Kingdom. [3]Alder Hey Children's Hospital, Liverpool, United Kingdom. [4]Loughborough University, Loughborough, United Kingdom

NHS England has established several Complications from Excess Weight (CEW) services. Despite physical activity (PA) being an integral part of successful weight management programmes, the capacity to offer an effective PA program within CEW services could be limited by resources. The aim of the study was to assess the feasibility of embedding an exercise specialist led, mobile health (mHealth) technology supported, PA and exercise intervention (MOTIVATE-CEW) to a CEW service. A 12-week feasibility, parallel group, randomised control trial was conducted in 23 adolescents with obesity (m/f $n=10/13$, age 15 ± 1y, SDS BMI 3.54 ± 0.54) receiving care from Alder Hey Children's Hospital (AHCH) CEW service. Participants were randomised to usual care (UC, $n=11$) or UC plus MOTIVATE-CEW ($n=12$). Participants receiving MOTIVATE-CEW co-designed a personalised progressive exercise and PA programme alongside an exercise specialist. The intervention was facilitated by mHealth technologies (smart watch, mobile app and coach's platform), which enabled remote exercise sessions and feedback guided by biometrics. A mixed method process evaluation assessed reach, dose and fidelity, and preliminary effectiveness was measured (health-related quality of life (HRQOL), body composition and cardiovascular disease risk factors). 45% of eligible participants were recruited and 87% completed post-intervention assessments. Recruited participants shared similar demographics to the AHCH CEW cohort for age, sex, and deprivation. A large effect size favouring MOTIVATE-CEW was observed for time spent completing moderate-to-vigorous intensity exercise per week (MOTIVATE-CEW 97 ± 127mins, UC 5 ± 12mins; d= 1.01), captured through optical heart rate monitoring. Qualitative perceptions of MOTIVATE-CEW were positive, key facilitators included regular personalised advice from an exercise specialist and the creation of graded action plans with specific behavioural goals. Data availability for in-clinic outcomes was good ($\geq85\%$). Preliminary evidence of moderate-to-large effects in favour of MOTIVATE-CEW were observed for HRQOL (EQ-5D-Y visual analogue scale; d=0.80), HDL cholesterol (d=0.67) and triglycerides (d=0.62). MOTIVATE-CEW demonstrated positive effects on exercise behaviour, suggesting that the addition of exercise specialists supported by mHealth technologies to CEW services would be an effective strategy to improve engagement in exercise and PA. Good reach and data availability suggests this study design is feasible for future trials.

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Oral Communications 9

OC9.1

Experience of the digital version of SEREN (Structured Education Reassuring Empowering Nurturing), Diabetes at Diagnosis module-improving paediatric diabetes care

Nirupa D'Souza[1], Rebekah Pryce[2], Yvonne Davies[3], Claire Baker[2], Julia Townson[4] & Josie Henley[4]
[1]Cwm Taf Morgannwg University Health Board, Bridgend, UK; [2]Cardiff and Vale University Health Board, Cardiff, UK; [3]Hywel Dda University health board, Carmarthen, UK; [4]Cardiff University, Cardiff, UK

Background
SEREN is an established, QISMET accredited structured education programme for children/young people (CYP) and their families with Type 1 diabetes mellitus (T1DM), developed in Wales. The first module 'Diabetes at diagnosis' has been in use in Wales since 2016. The resources and health care professional (HCP) training have also been used by some paediatric diabetes teams in England who have since embedded SEREN into their diabetes care. The education is ability banded and the resources are aligned with the school educational key stages. Creating a digital version to complement the face-to-face resources became possible in 2020, following a collaboration with the adult structured education programme BERTIE, which helped to pool resources and create a digital education platform for T1DM from infancy through to adulthood. The digital version of the SEREN face-to-face Diabetes at diagnosis module includes animations, videos and games. Funding from the 'Accelerate' programme enabled part of the development work and an evaluation by Cardiff University of the acceptability, initial impact and outcomes of this digital version.
Methods
CYP aged 11–14 years and their parents were recruited via the national diabetes Brecon Group register and contacted by their clinical teams. 11 CYPs took part. They had all been recently diagnosed with Type 1, received face to face education from their clinical teams using SEREN Diabetes at diagnosis (key stage 3) and accessed the digital version. 17 HCPs from across Wales and East Kent, England were also recruited. Semi-structured telephone-based interviews were carried out, recorded, transcribed and analyses conducted using a thematic approach.
Results
Overall CYP and their families and HCPs were positive in their feedback. They described the website as engaging and welcoming and saw it as complementary to the face-to-face resources. Several technical issues were detected and this information was used to improve the website. A Welsh translation is under development and further improvements will be made based on the evaluation. Future plans include extending the digital aspect of the modules to capture different learning styles of CYPs and their families, to ultimately improve self-management of diabetes and the long-term outcomes of T1DM

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OC9.2

Screening for paediatric type 1 diabetes – A qualitative study of parents and stakeholders

Naga Sai Manas Setti[1], Lauren Quinn[2], Thomas Horgan[1], Renuka Dias[3], Joana Garstang[4], David Shukla[5], Sheila Greenfield[6], Alex Richter[7] & Parth Narendran[2,8]
[1]College of medical and dental sciences, University of Birmingham, Birmingham, United Kingdom. [2]Institute of Immunology and Immunotherapy, University of Birmingham, Birmingham, United Kingdom. [3]Department of Diabetes, Birmingham Children's Hospital, Birmingham, United Kingdom. [4]Birmingham Community Healthcare Trust, Birmingham, United Kingdom. [5]Clinical Research Lead for Primary Care (West Midlands), National Institute for Health and Care Research; Clinical Research Fellow, Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom. [6]Institute of Applied Heath Research, University of Birmingham, Birmingham, United Kingdom. [7]Head of Clinical Immunology Service, University of Birmingham, Birmingham, United Kingdom. [8]Department of Diabetes, University Hospitals of Birmingham, Birmingham, United Kingdom

Objective
The EarLy Surveillance for Autoimmune diabetes (ELSA) study is screening 20,000 children aged 3-13 years for type 1 diabetes through measurement of islet autoantibodies. Screening aims to prevent diabetic ketoacidosis at clinical onset of disease and identifies the population who could benefit from prevention trials. The ELSA-1 study aimed to explore the perspectives of parents and stakeholders on the relative benefits and limitations of screening in the UK.
Methods
Semi-structured interviews were conducted with parents and stakeholders. The interviews were audio-recorded and transcribed. Interviews were conducted until data saturation was met and thematic analysis was undertaken using N-Vivo software to identify themes.
Results
Sixty interviews were conducted, including 33 family interviews (F) (36 parents and 14 children) and 27 stakeholder interviews (S) (6 general practitioners, 4 paediatricians and 6 stakeholders from non-healthcare settings). Overall, parents were supportive of screening ($n=33/36$). Parents cited the following benefits of screening; 1) better prepared for the future, 2) prevent emergency presentation at diagnosis and 3) monitoring follow-up to track progression. Concerns included the burden of 'living with risk' and harms of screening older children. There was emphasis on the education and support needed for families with children at-risk. The lack of preventative treatment negated the benefits of screening for a third of stakeholders. The major concern was around managing children at-risk within current NHS system pressures. Consensus guidelines for a monitoring programme were needed, including recommendations for management in primary and secondary care. Appropriate psychological support was also important for families with a child at-risk. Overall, screening stakeholders agreed screening was an important area of research.
Conclusions
ELSA-1 provides the first qualitative interview data in the UK to show that parents are supportive of screening and stakeholders recognise the importance of screening research. Barriers raised in ELSA-1 will be addressed through co-production workshops.

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OC9.3

A National Survey on the care and management of Children and Young people with Type 2 Diabetes

Suma Uday[1,2], Anjitha Anilkumar[3], Heather Clark[4], Anthony Walker[5] & Pooja Sachdev[6,7]
[1]Birmingham Women's and Children's Hospital, Birmingham, United Kingdom. [2]Institute of Metabolism and System's Research, University of Birmingham, Birmingham, United Kingdom. [3]University of Birmingham, Birmingham, United Kingdom. [4]West Midlands, Children and Young Person's Diabetes Network, Birmingham, United Kingdom. [5]Diabetes UK, Birmingham, United Kingdom. [6]Nottingham Children's Hospital, Nottingham, United Kingdom. [7]University of Nottingham, Nottingham, United Kingdom

Background
The National Paediatric Diabetes audit (NPDA) reports increasing number of children and young people with type 2 diabetes (CYP2D). CYP2D are less likely to receive all recommended health checks compared to those with type 1 diabetes (33% vs 59% respectively) and do not receive treatment for complications even when they are identified (T2D spotlight audit 2019/20). We assessed variation in care across different units against the national T2D guidelines.
Methods
A questionnaire concerning the management of CYP2D was distributed between December 2022- February 2023 to Paediatric Diabetes units across the UK.
Results
109 units (17, tertiary) responded, encompassing 824 patients. The majority of CYP2D were managed at District General Hospitals (DGHs) ($n=603$). The majority of units (75%) managed fewer than ten patients with T2D. Dedicated T2D clinics were reported by 13% ($n=12/92$) DGHs and 41% ($n=7/17$) tertiary centres. Blood pressure (BP) at each clinic visit was undertaken by 83% of units and rest measured it annually. The majority (73%) of units were able to initiate ambulatory BP monitoring when indicated. Following diagnosis of hypertension, 15% initiate treatment independently whereas 62% did so under specialist guidance; and 37% referred to a specialist. Tertiary centres were more likely to have a referral pathway for hypertension than DGHs (88% vs 16%, respectively). Obstructive sleep apnoea (OSA) screening was undertaken by 17% at diagnosis, 23% annually, 18% at each clinic visit and 42% occasionally. OSA pathway was available in 54% of units. Dyslipidaemia screening at diagnosis was undertaken by 93.6% and guidelines on treatment was available in 38%. Non-alcoholic fatty liver disease (NAFLD) screening was undertaken by 91% of centres(54% used liver function tests (LFTs) and 43% used both LFTs and liver ultrasound scan).
Conclusion
The majority of CYP2D are managed at DGHs with very few centres having dedicated T2DM clinics. Screening and management for hypertension, dyslipidaemia and NAFLD has improved since the spotlight audit. Tertiary centres were more likely to have referral pathways for identified co-morbidities.

Improving outcomes for CYP2D is one of the NHSE care priorities and the findings of the survey identifies key areas of improvement for future work.

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OC9.4

Evaluating the impact of a Health Care Assistant for care of children and young people with type 1 diabetes - "Improving the Time to Care"

Claire Hope, Gita Modgil & Giorgio Carrieri
Somerset Foundation Trust, Taunton, United Kingdom

Technological advances in the management of TIDM are making a significant impact on optimising blood sugar level control and improving quality of life for children with diabetes. Locally, the impact of technological advances, rising caseload and static numbers of Paediatric Diabetes Specialist Nurses (PDSNs) has led to a significant reduction in the 'time to care' as large amounts of clinic time was consumed by connections to technology and downloading by the diabetes team. We led a QI project looking at the impact of a healthcare assistant (HCA) in supporting the diabetes team and our families with the technology associated with their care. The HCA was able to support 484 new connections to technology and provide support for families in clinic, over the phone and take on numerous other administrative tasks. We demonstrated they released 23% of local total PDSN clinical hours; 274 hours of PDSN time over 10.5 weeks (1357 hours/year,) with a cost saving of £11,479/year compared to these tasks being managed by a Band 6 Specialist nurse. Both qualitative and quantitative feedback from CYP and their families was overwhelmingly positive; valuing the time the HCA could spend with them and stating gains in confidence with technology and preventing wasted time in clinic or repeat appointments. Feedback from the existing Diabetes consultants and PDSNs showed they felt they were able to focus their time better on direct clinical care and therefore able to optimise clinical decision making and clinics ran more efficiently. The HCA enjoyed their role and felt they were able to dedicate time to understanding the new advances in technology to support both the diabetes team and the CYP and their families. The success of the pilot has allowed us to receive ongoing funding for this role and we continue to see successes in this project on a daily basis.

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OC9.5

Impact of using hybrid closed loop system in a tertiary children's hospital: a single centre experience

Eman B. Kamaleldeen[1,2], Tabitha L Randell[1] & Pooja Sachdev[1]
[1]Department of Paediatric Endocrinology, Nottingham Children's Hospital, Nottingham, United Kingdom. [2]Pediatrics Endocrinology Unit, Department of Paediatrics, Faculty of Medicine, Assiut Universit, Assuit, Egypt

Background
Hybrid closed loop (HCL) insulin systems are associated with better glycaemic control and reduced hypoglycaemia risk. They represent the most advanced form of insulin delivery for people with type 1 diabetes mellitus (T1DM).
Aim
The study aimed to evaluate effectiveness of 3 HCL systems in children and young people (CYP) with T1DM at Nottingham Children's Hospital.
Methods
Data on HBA1c, TIR, hypo and hyperglycaemia three months before starting HCL and at 3, 6 and 12 months after HCL commencement were collected from Diasend® system (Glooko), Dexcom Clarity, and Care link (October 2019 - September 2022). Time in Hypoglycaemia (TIHo) and hyperglycaemia (TIHi) percentage were calculated as combination of percentage of low and very low and high and very high respectively.
Results
Patients on HCL $n=128$; 12-month data available for 98 patients. Mean age 10.5 (4.3) years, 65 boys (50%), diabetes duration 4.2 (3.8) years, 75% White British. Fourteen patients Medtronic MiniMedTM 780G, 30 CamAPS FX (CamDiab, Cambridge, UK), 82 Tandem Control-IQ AP system, 2 DIY Closed Loop (excluded).
Conclusions
Improvements in HBA1c, TIR, and time in hyperglycaemia were seen with HCL for 3 months & was sustained at 12 months in all 3 systems. Comparison within the 3 systems was not possible due to different numbers using each system and confounding factors such as eligibility for a particular system.

Table 1: Comparison between HbA1c, TIR, TIHo and TIHi percentage before and after HCL.

	3-month prior starting	3-month after starting HCL	6 months after HCL	12 months after HCL
Mean HbA1c (mmol/mol) (SD)	57 (9.7)	52 (7.3)	51.4 (7.1)	51.4 (7.1)
Mean TIR%	56.4	66.3	65.3	67.2
TIHo %	3.6	2.8	2.9	3.1
TIHi %	39.6	30.09	30.8	29.2

Table 2: Comparison between the three HCLs.

	Period after HCL (months)	780 G	Cam APS	Control IQ
Average HbA1c	3	54.6	51	51.9
	6	51.2	50.4	51.7
	12	59.3	50.5	50.5
TIR	3	73.9	63.2	66.1
	6	75.9	64.6	64.2
	12	73	69.3	66.6
% hypos	3	4	3.6	2.4
	6	4.2	3.7	2.5
	12	2.7	4.5	2.8
% hyperglycaemia	3	21.4	31.6	31
	6	18.8	30.1	32.9
	12	24.8	29.5	29.8

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OC9.6

How does HbA1c compare with OGTT in identifying patients with Diabetes Mellitus and Pre-Diabetes

Jack Sims, Chris Worth, Claire Manfredonia, Eleanor Ginbey & Mars Skae
Manchester Foundation Trust, Manchester, United Kingdom

Introduction
The incidence of Type 2 Diabetes Mellitus (T2DM) is rapidly increasing within the paediatric community, prompting searches for a simple and effective screening tool. Oral glucose tolerance test (OGTT) is the gold standard but is poorly accessible in the community. HbA1c offers an alternative which can be easily performed, but cut-offs for children have been extrapolated directly from the adult American Diabetes Association (ADA) diagnostic criteria. There is limited data for the accuracy of HbA1c as a screening tool in the paediatric population.
Aim
To assess the accuracy and utility of HbA1c as a DM screening tool against the gold standard (OGTT) in the paediatric population.
Method
Over five years, 70 patients undergoing OGTT at our hospital were found to have diabetes or pre-diabetes; 46 also had concurrent HbA1c tested. OGTT results classed as impaired fasting glucose (IFG, fasting plasma glucose $\geq$6.1 and $<$7 mmol/L), impaired glucose tolerance (IGT, 2hour plasma glucose $\geq$7.8 and $<$ 11.1 mmol/L) and diabetes mellitus (FPG $\geq$ 7 mmol/L or 2hPG $\geq$11.1) were compared with HbA1c categories as per ADA criteria.
Results
As can be seen in the table, there was no difference in HbA1c results between IFG, IGT and DM (defined by OGTT) groups (chi square = 3.94, $P=0.41$). The sensitivity of HbA1c for detection of DM was only 23%, with a specificity of $<$ 77%. Sensitivity of HbA1c for IFG and IGT was similarly low, at 48%.

OGTT diagnosis	HbA1c result		
	Normal	Pre-diabetes	Diabetes
IFG (n=7)	3 (43%)	3 (43%)	1 (14%)
IGT (n=26)	14 (54%)	10 (39%)	2 (8%)
DM(n=13)	3 (19%)	7 (44%)	3 (19%)

Conclusions
Our results demonstrate that ADA HbA1c cutoffs are insufficiently sensitive to identify those with pre-diabetes and T2DM in adolescent patients. It is likely that at the point of abnormal HbA1C detection in children, beta-cell reserve may be more significantly compromised with later detection of glycaemic dysfunction. OGTT must remain the screening test of choice for all paediatric patients at risk of dysglycaemia. Further analysis is required to determine accuracy of HbA1C thresholds specific to the UK paediatric population with more subtle glycaemic problems.

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OC9.7

Personalised carbohydrate prescriptions using individualised calculations prevent over prescribing carbohydrate to newly diagnosed children and young people with type 1 diabetes

Catarina Leal, John Pemberton & Anjanee Kholi
Department of Endocrinology and Diabetes, Birmingham Children's Hospital, Birmingham, United Kingdom

Introduction
The International Society for Paediatric and Adolescent Diabetes (ISPAD) 2022 Nutritional Guidelines recommend calculating carbohydrate requirements using an indivualised equation, such as the Schofield equation. Up to 2023, our centre used the Scientific Advisory Committee on Nutrition (SACN) 2011 guidelines that only require age to determine average carbohydrate requirements. The latest National Paediatric Diabetes Audit (NPDA) showed our centre to have 16.7% overweight and 28.5% obese CYPD, which is above the national average. Therefore, using ideal body weight (IBW) rather than actual body weight must be considered when calculating requirements.
Aim
To retrospectively compare the SACN carbohydrate requirements prescribed with individualised carbohydrate requirements calculated using the Schofield equation for newly diagnosed children and young people with type 1 diabetes (CYPD) at our centre.
Methods
Retrospective data analysis collected on newly diagnosed CYPD from January 2022 to December 2022. Anthropometric data [height, weight, age, Body Mass Index (BMI) centile] collected at diagnosis were obtained from our online diabetes management database (TWINKLE). SACN carbohydrate requirements were calculated by (1) Average energy requirements for age via SACN (2) 45% of energy from carbohydrates (3) divided by four to get grams (g) of carbohydrates. Schofield carbohydrate requirements were calculated by (1) Gender-specific Scofield equation to get energy requirement using IBW [BMI at the 50th percentile for age*(height in meter2)] with an activity factor of 1.5, steps (2) and (3) as above. Results are presented as mean (standard deviation) and mean comparisons using T-Test (two-tailed, $P<0.05$).
Results
There were 27 newly diagnosed CYPD with an average age of 9.6 (4.2SD) years, BMI of 19.2 (4.9SD) kg/m2, 67th centile, 44% being female. The average carbohydrate requirements using SACN and Schofield were, 257 (96.9SD) g and 185 (42.7SD) g, respectively. The SACN calculation suggesting 72 (72.9SD) g ($P<0.001$) more than the Schofield.
Conclusion
CYPD require an individualised carbohydrate prescription that uses height, weight, ideal body weight, and activity factor to prevent overprescribing carbohydrate. Our results support the ISPAD 2022 nutrition guidelines, and our practice has changed to tackle the high level of obesity in our cohort. Further audit will assess the impact of this change.

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OC9.8

CFTR modulators and glucose tolerance in children

Melissa-Sue Ryan[1], Kate Saunders[2], Anamika Saha[3], Andrew Prayle[4] & Pooja Sachdev[1]
[1]Paediatric Diabetes and Endocrinology, Nottingham Children's Hospital, Nottingham, United Kingdom. [2]School of Medicine, University of Nottingham, Nottingham, United Kingdom. [3]ESPE Clinical Fellow, Nottingham Children's Hospital, Nottingham, United Kingdom. [4]Paediatric Respiratory Medicine Group, University of Nottingham, Nottingham, United Kingdom

CFTR modulators are drugs that enhance/restore the expression, function, or stabilize the defective CFTR protein in patients with cystic fibrosis (CF). These modulators have shown marked improvements in lung function and quality of life for people with CF but their role in glucose tolerance is still unclear[1]. At Nottingham Children's Hospital, children with CF are eligible for kaftrio treatment (Elexacaftor/tezacaftor/ivacaftor CFTR modulator) from 10 years of age. We investigated if glucose tolerance improved after starting kaftrio.
Methods
The fasting glucose levels and 2hr OGTT levels 12 months prior to starting kaftrio, just before starting, and 12 months post treatment from 21 children and adolescents with CF (12 males) were compared. We also categorized the glucose response as normal, impaired, or meeting the criteria for CF-related diabetes to determine if categorical changes occurred with kaftrio treatment.
Results
Paired t-tests showed no overall significant difference between immediately pre-kaftrio fasting glucose and 12 months post kaftrio fasting glucose levels, $t(20)=1.4$, $P=0.166$. Likewise, there was no significant difference between the initial 2hr OGTT results and those 12 months after starting kaftrio $t(20)=0.4$, $P=0.663$. Comparing fasting glucose and OGTT levels from 12 months prior to starting to 12 months post-kaftrio treatment also showed no significant differences ($t(20)=1.8$, $P=0.089$ and $t(20)=0.5$, $P=0.595$, respectively). 15 patients remained with normal glucose tolerance after kaftrio treatment and one with impaired glucose tolerance (IGT). One patient went from IGT to normal glucose tolerance. In contrast, 4 patients moved to the CF-related diabetes category after kaftrio treatment.
Conclusion
This study showed no clear relationship between kaftrio treatment and glucose regulation in children. The majority of children in this study had normal glucose tolerance 12 months after starting CFTR modulator therapy. Longer term follow-up is needed to see if kaftrio delays the onset of impaired glucose tolerance known to occur with CF, in line with its protective function for pancreatic beta cells due to better activity of the CFTR protein.

[1]Merjaneh L. The role of modulators in cystic fibrosis related diabetes. Journal of clinical & translational endocrinology,2022,1;27:100286

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OC9.9

Quality improvement using PDSA cycles improves performance on NPDA key care processes for Birmingham Children's Hospital

Holly Wood[1], Lesley Drummond[1], Louise Collins[1], Donna Sands[1], Renuka Dias[1,2], Catarina Leal[1], Marie McElroy[1], Pauline Neylon[1], Ruth Krone[1], Melaine Kershaw[1] & John Pemberton[1]
[1]Birmingham Children's Hospital, Birmingham, United Kingdom. [2]University of Birmingham, Birmingham, United Kingdom

Background
From 2018 to 2020, the Birmingham Children's Hospital (BCH) Diabetes Team was a negative regional outlier for the National Paediatric Diabetes Audit (NPDA) seven key care processes. In 2021, the BCH team embarked on a Quality Improvement (QI) journey using Plan-Do-Study-Act (PDSA) cycles to improve care.
Objective
Review PDSA cycles of improvements from 2021 to 2023.
Methods
In 2021, the BCH team completed a national QI programme teaching PDSA cycles. The main change in 2021 was a revamped annual review clinic focussing on blood tests and care process delivery. In 2022, the review highlighted the annual review clinic only captured 60% of patients. Consequently, every clinic from May to September 2022 became an opportunity to target key care processes, focussing on annual screening blood tests and foot examinations, with reminders for arranging eye screening. The Operational Team reviewed the NPDA data quarterly, leading to data-driven adaptations of processes that the entire team embraced. This included phlebotomy attending the clinic, and regular clinic audits. We compared NPDA unit data for percentage completion of the seven individual key care processes for 2018, 2019, 2020, 2021 (COVID-19), 2022, and 2023 (unpublished). Additionally, we compared the percentage of those over 12 years of age with all seven completed processes for 2018, 2019, 2020, and 2021. Retinopathy screening national screening policy changed in 2021. Therefore, only the completion of six processes is reported for 2022 and 2023.
Results

Completion % /Year	2017-2018	2018-2019	2019-2020	2020-2021	2021-2022	2022-2023
HbA1c	99.6	100	99.6	82.4	95.3	98.4
BMI	99.1	100	99.2	70.2	93.6	98
Blood Pressure	97.7	100	98.5	69	91.5	97.3
Thyroid	73.1	77.7	73.6	65.3	78.8	89.3
Urinary microalbumin	53.5	66.9	63.5	33.9	70.2	85.7
Foot examination	74.4	79.0	83.9	59.3	75.2	93.9
Eye Screening	75.2	85.5	51.8	23.4	63.1	62.0
All 7 care processes for > 12 years	31.1	35.5	27.0	25.5	-	-
All 6 care processes for > 12 years	-	-	-	-	60.2	78.5

Conclusion
PDSA cycles and regular innovation moved the BCH team from a negative outlier from 2018 to 2021 to an above-average performer in 2022. The care process completion data for 2022-23 improved further.

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Oral Communications 10

OC10.1

The real-world experience of long acting growth hormone in children with growth hormone deficiency

Pon Ramya Gokul[1], Charlotte Jarvis[2], Peter Laing[2], Urmi Das[2], Renuka Ramakrishnan[2], Poonam Dharmaraj[2], Jo Blair[2], Mohammed Didi[2] & Senthil Senniappan[2]
[1]Alderhey Children's Hospital, Liverpool, United Kingdom. [2]Alderhey Children's Hospital, Liverpool, United Kingdom

Introduction
Long-acting growth hormone (LaGH) therapy has emerged as a newer treatment option for children, with the potential to improve adherence and compliance. Clinical trials have shown LaGH formulations to be effective and safe in children with GH deficiency (GHD). Somatrogon (Ngenla) is licensed for use in children with GHD over than 3 years of age.
Objective
We report the real-world experience of using once weekly Somatrogon (0.66mg/kg/week) injection in a group of children with GHD managed at a tertiary paediatric endocrine centre.
Methods
19 patients diagnosed with GHD (M:F,12:7, mean age of 5.78 years) were started on LaGH therapy. 5 patients were GH naïve, and 14 patients were switched from daily GH to LaGH therapy. Auxology, and IGF-1 levels (measured on day 4 after the weekly injection) at baseline and 3 months after starting treatment was analysed.
Results
All patients demonstrated a good, annualised height velocity (9.9cm/year) on LaGH therapy (average dose 15mg weekly). The mean IGF1 level improved compared to baseline and was within the normal range [baseline mean IGF1 levels was 15.54nmol/L, and post LaGH therapy was 28.1nmol/L. The patients preferred to continue the once-weekly LaGH injections in the long run due to the reduced frequency of injections and reported better adherence and improved quality of life. The weekly injections were tolerated well, and no side effects were reported during this period.
Conclusion
We report the real-world experience of using LaGH for the first time in the UK children with GHD, outside the trial setting. Our study provides early evidence highlighting the acceptance, safety, and effectiveness of LaGH in a routine clinical setting. Further longitudinal data in a larger group of patients would help to establish the long-term benefits, efficacy, and safety of LaGH.

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OC10.2

A multidisciplinary approach to the growth hormone shortage

Ross Burrows, Louise Foley & Claire Thirsk
Noah's Ark Children's Hospital, Cardiff, United Kingdom

In January 2023 a Medicines Supply Notification (MSN) was issued by the Department of Health and Social Care (DHSC) regarding a shortage of Norditropin (somatropin) products. The MSN recommended that all patients on Norditropin FlexPro 10mg pens and NordiFlex pens (all strengths) be changed to Omnitrope SurePal. Each patient affected by the shortage needed to be informed of the issue, a new prescription issued, and training provided on the new device. Affected patients were identified by the pharmacist and prioritised based on clinical need by their designated endocrinologist. The pharmacist wrote prescriptions for each patient and the patient's parents/carers were contacted by an endocrine nurse specialist or the pharmacist. The patient's family also received a letter explaining the situation with a QR code to the Omnitrope SurePal FAQ document. The homecare company was informed of all the patients needing training and parents/carer's email addresses were provided to enable virtual teaching by homecare nurses. Parent and carer feedback was collected electronically by Microsoft Forms and sent to their email addresses on their experience of the switch and using Omnitrope. 54% of all patients on growth hormone in the paediatric endocrine service were affected by this shortage. The majority (58%) were contacted and changed by the endocrine team within 14 days of the notice. The remaining patients were contacted within 21 days of the notice. Of those families contacted for feedback, 28 responded. 78% had changed to Omnitrope by April 2023, and 11% ran out of growth hormone before changing to Omnitrope. Once the stock issues with Norditropin have been resolved 88% would like to change back to their previous device. Clear communication and close working relationships within the multidisciplinary team enabled us to change every patient within 3 weeks of receiving the MSN. All affected patients were contacted, and the relevant paperwork was completed for the homecare company to change the patients to Omnitrope resulting in very few patients going without growth hormone. Patients are generally not happy with Omnitrope compared to Norditropin products and would prefer to change back to Norditropin when the shortage is resolved.

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OC10.3

Evaluating the impact of a nurse education refresher session for families who have a child with adrenal insufficiency

Louise Foley & Ross Burrows
Noah's Ark Children's Hospital for Wales, Cardiff, United Kingdom

Parents of children with adrenal insufficiency are taught to administer a hydrocortisone intramuscular (IM) injection in an adrenal crisis. This involves assembling a needle and syringe and drawing up a dose from a vial. It is known that parents report high confidence levels in administration of the injection but at the time of acute illness actual administration is poor. This study set out to see if introducing a planned refresher session for families would impact confidence levels, and increase the likelihood of parents administering the IM injection when needed, whilst also ensuring safety nets are up to date. The study consisted of three parts: A pre and post-questionnaire to assess parents understanding and confidence. Families were chosen at random filled out a pre-refresher questionnaire. Then asked to fill in a post-questionnaire 3-6 months afterwards. Emergency admissions were audited retrospectively to see if families who had attended a refresher were more likely to give the injection when indicated than families who had not attended a refresher. Audit of whether all safety nets were in place. 30 families completed the pre-questionnaire, and 16 of these families then completed the post-questionnaire. The refresher session demonstrated improved knowledge, and confidence levels remained increased 3-6 months afterwards. 100% of parents felt more likely to be able to give the injection. All parents wanted the opportunity to re-attend session. This was further demonstrated in hospital admissions, families were two times more likely give the IM injection appropriately after attending a refresher compared to those that did not. Safety nets were not up to date prior to the session, 44% of families did not have any hydrocortisone for injection and 50% needed needles and syringes. This study shows that refresher sessions improved the confidence and knowledge levels of families around when to give the IM injection, and increased the likelihood of them administering it when needed. It ensured the correct safety netting was in place. Going forward, patients will be offered 2 yearly refresher sessions. To improve the efficiency of the refresher sessions a Microsoft app has been developed to minimise administrative work associated with each session.

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OC10.4

The use of efmody (modified-release hydrocortisone, MRHC) in patients with congenital adrenal hyperplasia (CAH): initial experience and patient feedback

Alaa Baioumi[1,2], Sumana Chatterjee[1] & Elizabeth Crowne[1]
[1]Paediatric Endocrinology and Diabetes Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom. [2]Paediatrics Department, Ain Shams University, Cairo, Egypt

Background
Standard glucocorticoid therapy in CAH often fails to control androgen excess, causing glucocorticoid overexposure and poor health outcomes, particularly in adolescents. Efmody, a MRHC, has recently been licensed for CAH patients aged >12 years following a phase 3 study by Merke *et al*., 2021 demonstrating improved biochemical control in adults, steroid dose reduction over time, and patient-reported benefit.
Aim
To describe our initial experience of Efmody in CAH patients >12 years in a tertiary paediatric endocrine centre.
Methods
Retrospective clinical data was collected in CAH patients, started on Efmody since July 2022. Paired biochemical parameters before and 6 months post-treatment were either paired serum 17OHP, serum androstenedione, or capillary morning 17OHP levels.
Results
Efmody was started in 13 patients with salt-wasting CAH (69.2% females). Mean age and dose were 16.2 (range 12.1-20.7 years) and 11.8 (range 8.3-15.5

mg/m2/day) respectively. Paired biochemical data was available in 9/13 patients and 7/9 patients showed improvement in at least one of the parameters. Paired serum 17OHP levels were significantly lower post-treatment compared to baseline (19.9 vs 161 nmol/L, $P<0.05$) in 5 patients. Paired morning capillary 17OHP levels were significantly lower post-treatment compared to baseline (365.5 ± 268.2 vs 32.4 ± 28.8 nmo/L, $P=0.04$) in 4 patients. Paired serum androstenedione levels were significantly lower post-treatment (5.2 ± 5 nmol/L) compared to baseline 17.9 ± 10.9 nmol/L ($P=0.04$) in 5 patients. All 13 patients provided feedback in the clinic and 6/13 patients provided more detailed telephone feedback. 12/13 patients preferred twice daily dosing regimen particularly not having to dose during the day at school/college. 12/13 patients reported feeling better in the morning on Efmody. 3 females started on Efmody at 13 years started periods. Two patients found it inconvenient that they had to avoid eating in the evening after taking Efmody.

Conclusions

6 months of Efmody therapy improved 17OHP and androstenedione levels, also suggesting potential for reduction of overall glucocorticoid dose. Efmody was popular among adolescents because of convenience and feeling better in the morning. This supports the need for further systematic evaluation in a larger cohort.

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OC10.5

Parental perspective on genitoplasty for girls with virilising congenital adrenal hyperplasia

Arianna Mariotto, Supul Hennayake, Tamas Cserni, Indi Banerjee, Gail Busby, Mars Skae, Leena Patel, Raja Padidela, Philip Murray, Jaqueline Nicholson, Julie Jones, Charlotte Richmond & Anju Goyal
Manchester University NHS Foundation Trust, Manchester, United Kingdom

Introduction

In response to the proposed move to decommission genitoplasty surgery for DSD, we investigated parental views on surgery for girls with virilising 46XX Congenital Adrenal Hyperplasia (CAH).

Materials and Methods

In this prospective study, after ethical approval, parents of surgically treated CAH girls completed an electronic questionnaire.

Results

50 parents were contacted, 35 provided email address and 11 completed the questionnaires. Current median patients age is 13 (range 3-27) years. Genitoplasty done at median age: 12.7 (range 5-99) months. CAH had a negative impact on parental wellbeing (8/11); the condition had a positive effect on their bonding with child (6/11). Pre-surgery, the appearance of the genitalia reduced parental confidence in other carers (6/11) and reduced bonding with family members (3/11). Following surgery in infancy, 3 felt that the condition negatively affected their daughters' self-esteem and psychological wellbeing. Half of the parents found the decision for surgery challenging. Most (10/11) felt supported and well-informed by medical team and were satisfied with surgical outcomes. Only one would make different choice. The majority (8/11) disagreed with proposal to stop surgery, two did not give opinion and one agreed. Parent reported justifications for early surgery included avoidance of stigmatisation, reduced discomfort/anxiety, improved self-esteem.

Conclusion

The majority of parents (91%) were satisfied with their decision for surgery and 73% would prefer the option for early childhood surgery to be available. Parental responses suggested that following early childhood surgery, majority did not suffer from negative sequelae of differences in genital appearance. Results from a larger cohort will be required to confirm these findings.

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OC10.6

An appraisal on the quality and readability of growth hormone therapy patient information developed by paediatric endocrine societies

Jennifer McKechnie[1], Zhe Qian Ho[1,2], Avril Mason[1] & Sze Choon Wong[1,3]
[1]Department of Paediatric Endocrinology, Royal Hospital for Children Glasgow, Glasgow, United Kingdom. [2]School of Medicine, University of Glasgow, Glasgow, United Kingdom. [3]Department of Human Nutrition, University of Glasgow, Glasgow, United Kingdom

Background

In the UK, recombinant human growth hormone(rhGH) is approved for children with growth failure associated with six different conditions. According to NICE guidelines, clinicians should have a comprehensive discussion with patients and/or caregivers about treatment options. Research shows that patients retain only about 20% of the information provided during a consultation. This can be improved to around 50% when written information is also provided. Our study aimed to analyse the readability and quality of patient information on rhGH from major paediatric endocrine society websites.

Methods

We conducted a search on the websites of twelve paediatric endocrine societies to find patient/parent information leaflets on rhGH treatment, including its administration, monitoring, benefits, and side effects. We assessed the quality of the information using two validated patient information tools: the DISCERN instrument(16-items) and the EQIP tool(35-items). Readability was assessed with the Flesch reading ease score.

Results

We identified four patient information leaflets specifically designed for growth hormone treatment or general growth problems from four societies: Australia and New Zealand Society for Paediatric Endocrinology and Diabetes, European Society for Paediatric Endocrinology, Paediatric Endocrine Society and British Society for Paediatric Endocrinology and Diabetes. Median Flesch Reading Ease score was 57.2(range: 54–61.4) which is classified as fairly difficult to read. Median DISCERN score was 40.5 which is classified as fair quality (range: 21-58, maximum score 80), while the median EQIP score was 56 (range: 35-78, maximum score 100). All leaflets provided some description of the treatment purpose. Potential side effects were mentioned, but the benefits of treatment were not always fully described, and there were no quantitative estimates of risks or benefits. There was no indication that patients were involved in the production of any of the leaflets. While all leaflets had a satisfactory design, only one used clear figures or graphs, and only one provided a space for patients to take notes.

Conclusion

This study highlights the limited and suboptimal quality of available information on rhGH treatment through international paediatric endocrine society websites. The existing information may not adequately support patients and/or caregivers in making fully informed decisions.

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Posters

Adrenal 1

P1

Premature adrenarche and cardiometabolic risk – characterisation of a pilot cohort

Wogud Ben Said[1,2,3], Lucy Cooper[3,4], Ruth Krone[1,3], Shakila Thangaratinam[2,3], Wiebke Arlt[2,3,5] & Jan Idkowiak[1,2,3]
[1]Department of Endocrinology and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, Birmingham, UK; [2]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK; [3]Birmingham Health Partners, University of Birmingham, Birmingham, UK; [4]NIHR/Wellcome Trust Clinical Research Facility, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, Birmingham, UK; [5]UKRI MRC London Institute of Medical Sciences, London, UK

Introduction
Early-onset androgen excess commonly presents in pre-pubertal girls as premature adrenarche (PA). Girls with PA have clinical signs of androgen excess, such as pubic/axillary hair, body odour, greasy hair, and moderately elevated adrenal androgens before their 8th birthday. There is conflicting evidence if girls with PA are at higher risk to have or develop metabolic dysfunction, or progress to developing Polycystic Ovary Syndrome (PCOS), the most common complex metabolic condition in women of reproductive age.
Aim
We have launched a deep phenotyping study in children with premature adrenarche recruiting from our large, multi-diverse population. Herein, we report standard clinical cardiometabolic risk outcomes from our initial recruits.
Design and methods
Single-centre cross-sectional phenotyping study. We report on standard auxology and fasting biochemical parameters, including androgen profile (DHEAS [RIA], androstenedione [A4] and testosterone [T] [LC/MSMS]), fasting glucose, HbA1c and lipids (cholesterol, triglycerides).
Results
20 PA girls were included; precocious puberty and congenital adrenal hyperplasia were excluded clinically and biochemically. The age range is 5–8 years and 25% are of non-White British background. Median BMI z-score was +1.36 (range −0.5 – 2.55). All girls had elevated DHEAS (median: 3.14 µmol/L; range 1.3–5.6); in four girls, A4 was elevated above one-fold the upper limit of normal; in all, T levels were within the limit of normal. Median HbA1c was 33 mmol/mol (range 27–39), fasting glucose was 5 mmol/L (range 3.5–5.3); fasting cholesterol and triglyceride levels were within the normal range. Linear regression analysis showed a weak positive correlation between DHEAS and HbA1c (R2 0.25). No association was found between DHEAS and fasting glucose, DHEAS and lipids, DHEAS and BMI z-score, or BMI z-score with any metabolic parameters.
Summary and conclusion
Our pilot cohort of girls with PA is characterised by DHEAS excess. An unfavourable metabolic signature based on standard clinical parameters was not identified. Recruitment of children with PA and the establishment of a matched control cohort is ongoing, which will include in-depth biochemical assessment such as untargeted metabolomics and multi-steroid profiling.

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P2

Antenatal exposure to steroids, should we worry about neonatal adrenal suppression?

Khubaib Ahmed[1] & Umberto Piaggio[2]
[1]Leeds Children's Hospital, Leeds, UK; [2]Doncaster Royal Infirmary, Doncaster, UK

Background
Foetus is protected from high quantities of steroids by placental enzyme 11BHSD2. It converts steroids to inactive form (dexamethasone and betamethasone are exceptions). Exposure to high steroids for long time could saturate the enzyme. Maternal steroid use carries a theoretical risk for neonatal adrenal insufficiency (AI). The evidence remains controversial and most NICUs don't check for AI in those infants. Two units in south Yorkshire recommending synacthen test (SST) based on certain criteria. One of the units using antenatal dose thresholds of 7.5 mg/day prednisolone equivalent for ≥28 days while the other, 5 mg/day prednisolone equivalent for same duration as indication.
Aim
To test the relationship between antenatal steroid use and neonatal AI based on dose and duration set in the local guidelines.
Method
Retrospective cohort study in two centres. Term babies born to mothers on steroid who met criteria and had SST were included. cohort identified from laboratory data and results included cortisol levels at 0 then 30- and 60-minutes post-test. A retrospective notes review for dose and duration of steroid exposure, symptoms, and the outcome after test. Analysis used Spearman correlation coefficient between dose and duration of steroid exposure to test results respectively.
Result
Fifty-nine (59) patients were identified. Average dose of steroid used during pregnancy 19.7 mg prednisolone equivalent (none of the patients were exposed to dexamethasone or betamethasone). Steroids used for various autoimmune conditions in pregnancy. Average time of exposure of 173 days. Forty-eight (48) had full data for analysis. Five patients had abnormal SST, but none had clinical symptoms. There was no statistically significant correlation between dose and basal cortisol level ($P=0.51$) or peak cortisol response ($P=0.44$). Also, there was no statistically significant correlation between duration of exposure and basal cortisol level ($P=0.42$) or peak cortisol response($P=0.44$)
Conclusion
We recommend to revise the need for the guidelines based on current dose and duration of exposure. As the study did not include preterm babies, this cannot be generalised to include. We would still recommend low threshold for testing if clinical symptoms or in cases of prolonged exposure to dexamethasone or betamethasone.

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P3

Case series of non-classical congenital adrenal hyperplasia in childhood

Hannah Hickingbotham[1], Jessica Olivier[2], Priya Ramaswamy[1], Nazma Chowdhury[1] & Christina Wei[2]
[1]Croydon University Hospital, London, UK; [2]Evelina London Children's Hospital, Guys and St Thomas NHS Foundation Trust, London, UK

Introduction
Evidence in the management of children with non-classical congenital adrenal hyperplasia (NCCAH) is limited. We describe the clinical presentations and treatment of NCCAH patients under a tertiary paediatric endocrine centre.
Results
Data collected [reported in median(ranges)] identified 10(7M,3F) cases of NCCAH [21-hydroxylase deficiency(21-OHD)($n=9$), 11-deoxycortisol deficiency($n=1$)], aged 5.4(1.4–9.5) years at presentation. None had concurrent medical problems/treatment affecting steroid status. One asymptomatic male with a sibling with 21OHD, was diagnosed via genetics screening. 9 had bone age advancement (3.2(1.9–5.9) years), and >1 secondary sexual characteristic(s) at presentation: pubarche($n=9$), testicular enlargement(>4 mL) ($n=2$/7 M), breast development($n=2$/3 F), premature menarche(<aged 9y) (1/3 F). One female had clitoromegaly, labial fusion, but otherwise normal anatomy. At diagnosis, all had raised baseline 17-OHP(>3 nmol/L) of 56.2 (3.8–293) nmol/L, and a positive urine steroid profile (8/10) and/or positive genetics results (8/10). Synacthen stimulation tests (SST) reported 3 adrenal insufficiency (AI) (cortisol<300 mol/L), 3 partial adrenal insufficiency (pAI) (cortisol 300–420 nmol/L), 2 normal results. 7 patients (AI=3, pAI=2, normal SST=3) were started on daily hydrocortisone of 8.7(6.3–16) mg/m2/day at diagnosis. 1(F), post menarche at presentation and otherwise asymptomatic, was on sickness cover (30 mg/m2/day) for pAI (diagnosis SST peak cortisol 339 nmol/L, 408 nmol/L 1 year later). 1(M) initially on sickness cover for pAI needed maintenance HC after deterioration of SST (peak cortisol 257 to 88 nmol/L). 1(F) presented with pubarche and bone age advancement, had a normal SST requiring no steroids cover. She declined GnRHa for rapid pubertal progression, developed secondary amenorrhoea and was treated on Dianette. Positive LHRH tests for precocious puberty were reported in 3(2M,1F), 2(M) received GnRH analogues until 12y, and 1(F) post menarche was not treated.
Discussion
NCCAH in children often presents with adrenarche and bone age advancement. Testing of cortisol status is essential illustrated by the high prevalence of AI in our cohort. Steroid replacement is needed in patients with AI and should be considered if still growing with bone age advancement. However, the optimal dose requires further research.

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P4

Patient education for management of sick day episodes in adrenal insufficiency: A systematic review of published literature on structured education programs

Anna Bradford, A Mason & SC Wong
Department of Paediatric Endocrinology, Royal Hospital for Children Glasgow, Glasgow, UK

Background
Effective management of adrenal insufficiency (AI) during sick day episodes requires adjusting oral glucocorticoid therapy or administering intramuscular injections to prevent adrenal crises. Given the critical nature of adrenal crisis management, educating families of young individuals with AI is essential.
Aim
To critically appraise patient education concerning adrenal crisis management through a systematic review of structured education programs in the published literature.
Methods
We performed a systematic review in four databases (Medline, Embase, Web of Science, CINAHL). Our key research questions were:
- What structured educational programs exist for patients with adrenal insufficiency concerning the management during sick day episodes?
- How effective are these structured educational programs?

The systematic review was conducted in accordance to the PRISMA 2020 guidance. Eligible papers were fully reviewed and data extracted using a standardised proforma with focus on details of the structured programme, the patient population and efficacy of the program.
Results
The systematic literature search yielded three publications involving a total of 795 patients. Two publications were structured education programs in Europe (The Netherlands and Germany), whilst the third was in United States of America. Two publications included patients with a variety of underlying aetiologies of primary and secondary AI whilst the third involved patients with breast cancer who had undergone bilateral adrenalectomy as part of treatment. All of these three structured educational programs involved adult patients and were delivered face to face. Two programs were conducted by endocrinologists and endocrine nurses (a 2-hour small group training session and a 3-hour educational meeting), while one program was led by pharmacists (a three-step program taught over 3 consecutive days). All programs included opportunities for practicing injection techniques and resulted in improved knowledge and patient satisfaction based on patient questionnaires.
Conclusion
Limited evidence exists in the published literature regarding structured educational programs for patients with AI, with none specifically tailored to paediatric patients and their families. There is a crucial need to understand the educational requirements of families and young individuals with AI to develop accessible educational resources and programs in collaboration with them.

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P5

Retrospective review of patients with 21-hydroxylase deficiency (21OHD) Congenital adrenal hyperplasia (CAH) in a tertiary children's hospital

Katherine Riches[1], Rose Abey[1], Louise Denvir[2], James Law[2] & Pooja Sachdev[2]
[1]University of Nottingham, Nottingham, UK; [2]Queen's Medical Centre, Nottingham, UK

Background
The most common form (90%) of CAH is 21-hydroxylase deficiency (21OHD). Management is with hydrocortisone ±fludrocortisone replacement while minimising side effects of androgen excess. Our aim was to review our CAH cohort and describe their characteristics, treatment regimens and growth.
Methods
Retrospective data on height, weight, BMI, bone age and biochemical profiles was collected on 26 patients with 21OHD (19 females and 7 males) between June 2021 and January 2023.
Results
Initial presentations included ambiguous genitalia (56%), precocious puberty (16%), adrenarche (15%) and salt-wasting (8%). Patients were reviewed clinically every 6 months on average and all patients had an emergency sick day plan in place. Patient characteristics are outlined in Table 1. 84% of patients were on a total daily hydrocortisone dose of 10–15 mg/m^2 per day with the highest dose typically given in the morning. Younger patients received a higher dose of fludrocortisone. 17-OHP and androstenedione were most frequently requested. Testosterone, renin and aldosterone were less consistently requested. Salivary 17-OHP was undertaken on 6/26 patients (23%). Bone ages were advanced with both salt-wasting (+1.46±2.55 SDS) and non-salt-wasting (+1.41±1.21 SDS) and markedly advanced in 2/4 patients not on hydrocortisone treatment (+2.93±2.11).
Discussion and conclusion
The majority of patients were on recommended doses of hydrocortisone. Two out of four of the patients not on hydrocortisone treatment (normal synacthen) had significantly advanced bone ages but height was not compromised. One of the patients was on anastrozole treatment only. Renin ± aldosterone was requested in 46.7% of patients on fludrocortisone but did not result in changes to treatment even when results were outside the reference range. 17-OHP salivary profiles were less frequently requested than blood 17-OHP, but allowed targeted treatment adjustments and should be considered a routine part of management in CAH.

	Salt wasting	Non-salt wasting	*Not on hydrocortisone treatment
Number	15	7	4
Total daily dose HC (mg/m^2 per day) median (IQR)	13.08 (2.94)	12.7 (1.93)	
Morning dose HC as % of TDD median (IQR)	37.5 (11.32)	36.4 (7.42)	
Bone age SDS (mean/S.D.)	1.46±2.55	1.41±1.21	2.93±2.11
BMI SDS (mean/S.D.)	0.96±1.20	2.08±3.22	1.38±2.36

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P6

Bone mineral density in children with congenital adrenal hyperplasia presenting to tertiary care hospital from LMIC

Karishma Rahak, Versha Rani Rai, Professor Mohsina Ibrahim & Roshia Parveen
Pediatric Endocrine Department, National Institute of Child Health, Karachi, Pakistan

Background
C Treatment in all forms of CAH includes lifelong replacement of steroids. Steroids have an impact on bone health in multiple ways and are known to cause osteoporosis when given in high doses or for a longer duration.
Objective
To evaluate bone mineral density (BMD), using dual-energy X-ray absorptiometry (DEXA) scan in children with CAH taking long-term steroids presenting in the pediatric endocrinology ward of National Institute of Child Health, (NICH) Karachi, Pakistan.
Materials and methods
This cross-sectional study was performed at the Department of Pediatric Endocrinology, National Institute of Child Health, Karachi from October 2021 to July 2022. A total of 47 diagnosed cases of CAH taking steroids for more than 5 years were enrolled. Assessment of BMD was done using a DEXA scan. Lumbar spine BMD was done and Z-score was modified for height for age z-score. The dose of steroids and duration was calculated.
Results
Out of 47 patients, low BMD was observed in 8 (17.02%) patients. Individuals with low BMD had significantly higher median duration, ($P=0.017$), dose ($P=0.003$), and median alkaline phosphate level ($P=0.036$),) but low median BMD value ($P=0.009$) and z score ($P<0.001$) than normal BMD individuals. Although median bone age ($P=0.009$) was appropriate for chronologic age in low BMD patients. A moderate negative significant correlation was observed between z score and age (rho = −0.319, $P=0.029$), z-score and duration of steroid treatment (rho = −0.364, $P=0.012$), z score and alkaline phosphate (rho = −0.466, $P=0.001$), z score and bone age (rho = −0.378, $P=0.009$).
Conclusion
Low BMD was observed in 17% of children on the DEXA scan. Moreover, these individuals had significantly higher median average duration and dose of hydrocortisone.
Keywords
Bone Mineral Density (BMD), Congenital Adrenal Hyperplasia (CAH), Dual Energy X-Ray Absorptiometry (DEXA).

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P7

CortiCit: Development of a hydrocortisone intramuscular injection kit for adrenal crisis

K Lynette James[1,2], Ross Burrows[3], Louise Foley[4], Angela Hallam[5], Amelia Huw Morgan[6], Delyth HigmanJames[7], Rebekah Pryce[4], Catherine Talbot[5] & D Aled Rees[8,9]
[1]Pharmacy Department, Cardiff and Vale University Health Board, Cardiff, UK; [2]Cardiff University, Cardiff, UK; [3]Pharmacy Department, Noah's Ark Children's Hospital for Wales, Cardiff, UK; [4]Noah's Ark Children's

Hospital for Wales, Cardiff, UK; [5]St Mary's Pharmaceutical Unit, Cardiff and Vale University Health Board, Cardiff, UK; [6]Cardiff Metropolitan University, School of Art and Design, Cardiff, UK; [7]Cardiff Metropolitan University, Cardiff School of Sport and Health Sciences, Cardiff, UK; [8]Neurosciences and Mental Health Research Institute, Cardiff University, Cardiff, UK; [9]Department of Endocrinology, Cardiff and Vale University Health Board, Cardiff, UK

Adrenal crisis (AC) is a life-threatening episode of adrenal insufficiency (AI) resulting from impairment of glucocorticoid secretion by the adrenal cortex. Approximately 1 in 200 patients die from AC annually.[1] AC is often precipitated by intercurrent illness, injury or surgery and can be prevented by increasing oral corticosteroid doses ('stress dosing') during illness. Parenteral hydrocortisone may be necessary if oral therapy cannot be absorbed or ineffective. Patients and/or carers are instructed to carry and administer intramuscular hydrocortisone in an emergency. Research demonstrated that 47% of children and 67% of adult patients carried parenteral hydrocortisone, with 12% and 22% respectively using their injection during acute illness.[1] This study aimed to examine and address the barriers to patient use of emergency intramuscular hydrocortisone. Three virtual focus groups were conducted, via Zoom, involving 14 patients with AI (group 1 = 7; group 2 = 2; group 3 = 5). Audio-recordings were transcribed verbatim and analysed thematically. Participants highlighted challenges obtaining hydrocortisone ampoules and ancillaries from general practitioners to create kits. The availability of videos and pictorial leaflets describing the process of administering hydrocortisone injections were deemed valuable in supporting training of patients/relatives. CortiCit is a bespoke hydrocortisone intramuscular injection kit developed by endocrinology and pharmacy colleagues at Cardiff and Vale University Health Board. The paediatric and adult kits are manufactured specials containing two ampoules of hydrocortisone sodium phosphate 100 mg/mL, syringes and needles. A bilingual illustrated instruction leaflet, co-produced with the focus group participants and Cardiff Metropolitan School of Art and Design, is included within the kit. The leaflet has a QR code linking to a bespoke video on administering the injection. CortiCit also contains the age-appropriate national emergency steroid therapy card. The CortiCit is prescribed on hospital discharge and outpatient prescriptions across Wales, with a view to extending to GP prescribing at a later date. The CortiCit has been well received by patients/relatives with formal evaluation findings pending. The study highlights the importance of multi-disciplinary collaboration to co-produce a hydrocortisone kit that fulfils patient needs.

1. Eyal O et al. Adrenal crisis in children with adrenal insufficiency epidemiology and risk factors. *Eur J. Pediatr.* 2019;178:731–738

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P8

When management becomes the source of my sorrow! (prolonged steroids' side effects and adrenal insufficiency from the patient's perspective)

Mai Ali
Leeds General Hospital, Leeds, UK

Introduction
An overview of a 14-year-old Duchenne muscular dystrophy patient who was subjected to steroid treatment and suffered greatly as a result. This case study illustrates how management effects can occasionally have a negative impact on our bodies via the lens of a patient. This event also shows that what's important to patients might not always be the same as what's important to medical professionals.
Case history
This case study features E, who has Duchenne muscular dystrophy, confirmed genetically at the age of 21 months. He was chosen to participate in the For-DMD study when he became 4 years old. According to the experiment, he was randomly allocated to take daily deflazacort (0.9 mg/kg per day). After a few years, it became apparent that E was experiencing a variety of endocrine side effects from using steroids, chief among them being adrenal insufficiency, which was discovered by a very low morning cortisol level. E's mother consequently completed a series of sessions to ensure she was equipped to provide a steroid injection if required.
Due to prolonged steroid use
E has short stature and decreased bone density indicated by successive DEXA scans, which supported the conclusion that E suffered fractures brought on by osteopenia. The significant back pain and the fact that E's mother feels depressed and unable to hide it on his bedside when he was in the hospital because she cannot find a parental room to cry alone when E cannot see her were the worst effects on E, in his opinion. Other side effects included delayed puberty. Speaking with E, it was clear how happy he felt when he began displaying some secondary sexual traits in response to testosterone gel therapy. Numerous additional endocrinological problems brought on by steroid use and adrenal insufficiency were also identified and reported. Remarkably, the taste of the pills was among the worst he ever encountered.
Conclusion
E's continued autonomy and participation in his management strategy are what, in the end, satisfy him.

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P9

First case recognized as autoimmune polyglandular syndrome type 2 with double seronegative myasthenia gravis – A case report-from Pakistan

Maira Riaz[1], Versha Rani[2], Mohsina Ibrahim[3] & Zubair Khoso[2]
[1]National Institute of Child Health, Karachi, Pakistan; [2]Natioanl Institue of Child Health, Karachi, Pakistan; [3]National Institute of Child Health, Karachi, Pakistan

Autoimmune polyglandular syndrome type 2 (APS-2) is cluster of autoimmune diseases characterized by autoimmune adrenal insufficiency and thyroid disease (Schmidt' syndrome) with or without type 1 diabetes (carpenter syndrome). This autoimmune condition may be associated with hypogonadism, hypopituitarism, immunoglobulin A deficiency, myasthenia gravis, celiac disease, and vitiligo. Co-existence of myasthenia gravis and APS 2 is extremely rare and their common etiology has been unclear Here, we report a case of APS2 accompanied by congenital myasthenia gravis and focal segmental glomerulosclerosis. A 2 year, 5-months old girl, known case of adrenal insufficiency since the age of 9 months and hypothyroidism since the age of one and half years. She also had been treated for steroid resistant nephrotic syndrome due to focal segmental glomerulosclerosis since age of 18 months Now presented with complaint of bilateral ptosis and cough for last 2 months. On examination, Well oriented child with obvious bilateral ptosis with weight (−1 SDS) and height (−2SDS),BP above 99th centile and no sign of dehydration and pigmentation and other systemic examination was unremarkable and normal female genitalia with prepubertal Tanner stage. On investigation Electromyography (EMG) and nerve conduction studies showed myopathy. Serum anti-Anti acetylcholinesterase receptor antibodies and serum Anti MuSK Antibodies titer were negative. HRCT showed no evidence of thymoma. Pyridostigmine started for seronegative myasthenia gravis and during treatment patient improved. APS type 2 is associated with genetic abnormalities of class II HLA alleles with HLA-DR3 and/or HLA-DR4 haplotypes. APS type 2 has a male-to-female ratio of 1:3. Although cases of APS-2 have been reported in children. Its association with myasthenia gravis is rare, and their existence with focal segmental glomerulosclerosis has not been reported until now. So, given predilection to concomitant diseases, regular surveillance is crucial to screen for other conditions. Hence, this case report is very important since it recollects all the information needed for the prompt diagnosis and the corresponding management that physicians need to know for the adequate treatment of the patients suffering from this condition

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Bone 1

P10

LC–MS/MS measurements of serum zoledronate in children and young people receiving treatment – findings from the Moving Towards Individualised BisphosphonatE Therapy (TIBET) study

Tabitha Bartlett[1], Jonathan C Y Tang[1,2], Rachel Dunn[1,2], Sharan Subramanian[3], William D Fraser[1,2] & Emma Webb[2,3]
[1]Bioanalytical Facility, Norwich Medical School, University of East Anglia, Norwich, UK; [2]Clinical Biochemistry, Departments of Laboratory Medicine and Departments of Diabetes and Endocrinology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [3]Jenny Lind Children's Hospital, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK

Background
Zoledronate is a nitrogen-containing bisphosphonate (BP) recognised for its antiresorptive potency. The pharmacokinetic/pharmacodynamic of zoledronate remains unclear. Although adverse events from overuse of BP is rare, there have been reports of over-treatment resulting in pathophysiological consequences. The current administration regimen is not tailored to the individual's therapeutic

response to zoledronate. Quantifying post-dose serum concentrations could improve drug monitoring and reduce over-treatment.
Method
A high-throughput liquid chromatography tandem mass spectrometry (LC–MS/MS) method for the quantification of zoledronate in human serum was developed, validated, and applied to samples collected for the TIBET study (IRAS:292768). The study recruited pediatric patients who had received zoledronate doses ranging between 0.02–0.05 mg/kg 4–6 months ago. Serum samples ($n=16$) were obtained with parental consent and stored at $-20\,^{\circ}C$ until analysis. Participants age ranged between 3–17 yrs consisted of 9 males and 7 females with various diagnoses including OI and Duchenne muscular dystrophy. Sample analysis was performed using a triple quadrupole mass spectrometer system (Sciex API4000, Macclesfield, UK). Solid phase extraction using 96-wells weak anion exchange (WAX) plates were processed using an automated platform (Biotage Extrahera, Sweden) to remove sample matrix components.
Results
The zoledronate assay achieved adequate linearity across the range of 35–900 nmol/L and showed intra/inter-assay precision(CV%) of $<9.0\%$ and $<12.3\%$. The lower limit of quantification (LLoQ) was 35.0 nmol/L and recovery was 99.3%. Zoledronate was detected in all 16 patient samples; three samples had quantifiable concentrations above the LLoQ between 67.8 to 114.4 nmol/L. The highest zoledronate concentration was found in a sample collected 4-months post infusion compared to an average of 6-months. Our findings showed residual amounts of zoledronate were present in circulation long after the expectant half-life, indicating variable responses in absorption into the bone and that differences in excretion may result in zoledronate remaining in the systemic circulation.
Conclusion
We have shown that our LC–MS/MS method can be used to determine zoledronate concentrations in patients post intravenous infusion. We report variable concentrations of zoledronate likely due to individual differences in absorption/excretion. A better understanding of zolendronate pharmacokinetics could enable personalised treatment plans, reducing the risk of under/over-treatment.

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P11

Assessment of children's bone health: Establishing paediatric reference (prefer study) values for 1,25 vitamin D

Amrou Farag[1], Jonathan C Y Tang[2,3], Rachel Dunn[2,3], Allison Chipchase[3], William D Fraser[2,3,4] & Emma Webb[5]
[1]University of East Anglia, Norwich, UK; [2]Bioanalytical Facility, Norwich Medical School, University of East Anglia, Norwich, UK; [3]Clinical Biochemistry, Departments of Laboratory Medicine, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [4]Departments of Diabetes and Endocrinology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [5]Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK

Background
The active form of vitamin D, $1,25(OH)_2D$, plays a key role in regulating calcium and phosphorus metabolism and bone homeostasis. In paediatrics, maintaining optimal $1,25(OH)_2D$ levels is crucial for supporting musculoskeletal growth. The hormone also serves as a diagnostic indicator for multiple disorders such as vitamin-D dependent rickets. Current Literature lacks comprehensive reporting of age-specific reference ranges in paediatrics. Immunoassays have traditionally been used, but the antibodies have variable affinities to both $1,25(OH)_2D_2$ and $1,25(OH)_2D_3$ and can cross-react with circulating isomers of vitamin D. We have developed an LC–MS/MS method to measure $1,25(OH)_2D$ concentrations with greater specificity than immunoassay and have established age-specific ranges for a healthy paediatric cohort.
Methods
Written informed consent was taken from healthy children aged 0 to 16 years attending a tertiary centre for a planned surgical procedure. Fasting serum samples were collected, and calcium intake and medical history recorded. Serum $1,25(OH)_2D$ concentration was measured by immunoassay (Diasorin LIAISON XL) and LC–MS/MS (Waters Xevo TQ-XS). Assay performance was compared via regression analysis. Parametric tests were used to assess the statistical significance of differences in $1,25(OH)_2D$ levels to inform age and sex partitioning.
Results
375 individuals (mean age 7.5 ± 4.5 years S.D.) and were included in the analysis. The measurements obtained by immunoassay (mean: 134.8 ± 37.6 pmol/L S.D.) were higher than those by LC–MS/MS (mean: 124.9 ± 37.8 pmol/L S.D.). Regression analysis revealed a moderate linear relationship between both methods ($y=0.8x+15.4$, $r^2=0.65$). All ranges were reported as 95% confidence intervals (CIs). Reference ranges were independently reported for four age groups: 0 to <3 3 to <7, 7 to <13, and 13 to <15. Sex partitioning was needed for those aged 13 to <15. There was no significant impact of gender at all other ages. $1,25(OH)_2D$ concentrations were found to be affected by seasonal variation.
Conclusion
Diasorin immunoassay measured concentrations were significantly higher than the new LC–MS/MS method. This is believed to be secondary to differences in assay specificity to $1,25(OH)_2D$. Establishing age-specific normative data for $1,25(OH)_2D$ using LC–MS/MS data will provide more accurate reference ranges for the paediatric population.

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P12

Impairment of muscle mass and muscle function in osteogenesis imperfecta: A systematic review

Caleb Hariri[1], Jennifer McKechnie[1], Avril Mason[1] & Sze Choong Wong[1,2]
[1]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [2]Department of Human Nutrition, University of Glasgow, Glasgow, UK

Objective
This systematic review aimed to identify and analyze skeletal muscle outcomes in patients with osteogenesis imperfecta (OI), a condition characterized by structural and metabolic abnormalities in skeletal muscle. Specifically, the review focused on assessing muscle mass and function using various imaging modalities.
Methods
A systematic search was conducted in MEDLINE and EMBASE databases. Inclusion criteria comprised patients with any type of OI, measurements of muscle mass using any imaging modality, and assessment of muscle function.
Results
A total of five publications involving a total of 436 patients (age range: 4.8–21.3) met the inclusion criteria. Among these, three were case control studies: one examined lower limb muscle using peripheral quantitative computed tomography(pQCT) and lower limb mechanography(type I OI), another utilized forearm pQCT and DXA to assess total body lean mass(type I, III, and IV OI), and the third evaluated grip strength and lower limb mechanography(type I and IV OI). Additionally, one study compared DXA total body lean mass (type I and IV OI) with normative data derived from a group of healthy controls, while the last study focused on a clinical trial of whole-body vibration therapy in type I and IV OI, comparing DXA total body lean mass, lower limb mechanography, and the 6-minute walk test with normative data. Overall, all papers provided evidence of deficits in muscle mass and function in OI across multiple sites, including the calf, forearm, and total body lean mass. No statistically significant differences were found between OI subtypes for any of the outcomes, although one study reported no significant differences in pQCT forearm muscle mass between type IV OI and healthy controls.
Conclusions
This systematic review establishes that children and adults with OI exhibit deficits in skeletal muscle mass and function, as evidenced by multiple studies utilizing various imaging modalities. The inclusion of clinically relevant muscle outcome measures, along with patient engagement, is crucial for both clinical practice and clinical trials. Furthermore, additional clinical studies focusing on understanding the underlying basis of skeletal muscle deficits may help identify targets for therapy and improve muscle outcomes in individuals with OI.

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P13

Cessation of burosumab treatment in adolescent patients with XLH: A multi-centre case series

Suma Uday[1], Charlotte Jarvis[2], Renuka Ramakrishnan[2], Talat Mushtaq[3] & Angela Williams[4]
[1]Birmingham Women's and Children's Hospital, Birmingham, UK; [2]Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [3]Leeds Children's Hospital, Leeds, UK; [4]Kyowa Kirin International PLC, Marlow, UK

Background
X-linked hypophosphataemia (XLH) is a genetic condition that causes significant skeletal deformities and is associated with lifelong disability and pain. In October 2018, the NHS in England recommended burosumab, an anti-FGF23 antibody, for treating XLH with radiographic evidence of bone disease in children aged 1 year and over, and in young people with growing bones. The clinical and cost effectiveness of burosumab for treating adults with XLH is being assessed.

Purpose
There is a lack of data reporting outcomes in patients who have experienced cessation of burosumab therapy at the end of bone growth. This multi-centre case series shares real-world experience of burosumab cessation in such patients.
Methods
Descriptive report of four patients with XLH from three centres in England. Medical history and biochemical and radiological findings, as well as patient and caregiver experiences, are reported.
Results
Two female patients were diagnosed prior to symptoms, having had a family member with a confirmed *PHEX* mutation, two (one female, one male) were diagnosed in early childhood (2 and 5 years old, respectively) after presenting with symptoms. All patients initially received conventional therapy (oral phosphate and active vitamin D). Symptoms during this time included skeletal deformity, pain, stiffness, gait disturbance, limited mobility and psychological effects. All patients were switched to burosumab and were treated for 2–4 years until the end of growth. During this time, one patient was reported as demonstrating leg straightening. Patients had improvements in bone biochemistry markers. Patients reported quicker recovery from orthopaedic surgery than when they were on conventional therapy, reduction in pain and stiffness, improved mobility, higher energy and activity levels, and improved school attendance. Following cessation of burosumab at the end of bone growth, patients subsequently reported experiencing more pain, less energy, reduced mobility and consequences on work and psychological wellbeing. Two of the patients had been changed back to conventional therapy.
Conclusion
These cases provide some insights into patient course after cessation of burosumab at the end of bone growth. Stopping treatment led to symptom recurrence and reduced patient wellbeing, suggesting that re-initiation of treatment may be warranted.

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P14

Clinical utility of individual biochemical markers in screening for metabolic bone disease of prematurity

Eman Elmeligy[1] & Amish Chinoy[2]
[1]University of Manchester, Manchester, UK; [2]MRI Paediatric Endocrinology, Manchester, UK

Introduction
Metabolic bone disease of prematurity (MBDP) is a common condition in preterm and low birth weight infants, characterised by under-mineralisation of bone due to inadequate mineral supply, which can increase the risk of fractures. Screening is undertaken using biochemical markers, typically serum phosphate (PO4), alkaline phosphatase (ALP) and parathyroid hormone (PTH), although the objective clinical utility of these markers individually has not been explored.
Objective
To investigate the utility of the biochemical screening markers for MBDP by determining sensitivity, degree and timing of derangements.
Methods
All preterm infants admitted to a tertiary neonatal unit over a one-year period that had biochemical evidence of MBDP (at least one of: raised ALP, raised PTH and low PO4) with no other explanation for derangement were included, with the progress of their biochemistry tracked retrospectively.
Results
59 preterm infants were included. The mean age for the first derangement of each marker was 23 days for ALP, 40 days for PTH, and 24 days for PO4. Peak derangement was noted earlier with PO4 (39 days) than PTH (65 days) and ALP (56 days). PTH demonstrated the greatest degree of derangement – average peak value 16.2 pmol/L (standard deviation 12.8, upper limit of normal 6.9). Sensitivity for predicting MBDP was 81% for ALP, 78% for PTH and 71% for PO4, with the greatest sensitivity achieved with a combination of raised ALP and PTH (98%). However, at the time of first screening for MBDP, sensitivity for predicting future derangements was 59% for ALP and PTH, and 39% for PO4. Earlier derangements were observed to ALP and PO4 than PTH, particularly in extremely preterm or extremely low birth weight infants.
Conclusion
Biochemical derangements of MBDP are noted from 3–4 weeks of life, suggesting that screening should commence from this point. A combination of PTH and ALP provides the greatest sensitivity for predicting MBDP.

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P15

Stuve Wiedemann syndrome – case series of 3 cases

Bharani Anand Ramalingam, Bindu Avatapalle, Georgina Williams & Rebekah Pryce
University Hospital of Wales, Cardiff, UK

Introduction
Stuve–Wiedemann Syndrome (SWS) is a rare genetic condition with autosomal recessive inheritance characterized by the association of typical facial appearances, skeletal manifestations including bowed legs and dysautonomia. Only two patients with long survival have been reported in 2001. We report three children whose periodic clinical evolution could be observed in our hospital until the age of 9 years. We report a case of SWS with associated nephrotic syndrome – a previously unrecognised association.
Case 1
A female child born to consanguineous parents with short limbs and talipes. Required initial period of ventilation. She had feeding difficulties and experienced episodes of hyperpyrexia and increased sweating. She was diagnosed with the expertise of the European skeletal dysplasia network as the initial CGH was not contributory.
Case 2
The brother of case 1, had signs of PPHN which settled postnatally. He had a cardiac arrest, during which he developed rhabdomyolysis with acute renal failure. He had severe keratitis compared to his sister, both had osteopenia and scoliosis and were supplemented with Vit-D and alpha calcidol
Case 3
Sixth-born male child to non-consanguineous parents with antenatally diagnosed bent long bones. He had a similar clinical profile characteristic of Stuve Weidemann syndrome with skeletal dysplasia and dysautonomic symptoms and confirmed LIFR gene mutation. He has superior end plate fractures from T10-L1 and 2 fractures in right fibula and middle finger with trivial trauma awaiting DEXA prior to consideration of Bisphosphonates. He has a scoliosis and abnormal gait with apparent limb length discrepancy with valgus deformity. He developed steroid-dependent nephrotic syndrome which is not a described association of SWS. LIFR gene mutation is associated with urogenital anomalies with urothelial changes, but nephrotic syndrome has not been described before in the literature. The initial steroid treatment may have contributed to osteopenia.
Conclusion
SWS is a rare condition in which osteopenia and the use of Bisphosphonates is postulated to be beneficial. However, international collaborations to develop multi-disciplinary expertise and clinical recommendations would be beneficial.

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P16

Infantile hypocalcemic seizures secondary to maternal vitamin D deficiency followed by persistent hypomagnesemia

Vinyasa Kolli, Alagusutha Jeyaraman & Sanjay Gupta
Hull Royal Infirmary, Hull, UK

Background
Infants born to mothers who are deficient in vitamin D are at risk of developing vitamin D deficiency and hypocalcaemia.We present a case report on infantile hypocalcemic seizures secondary to vitamin D deficiency followed by persistent hypomagnesemia.
Case description
A 4-week-old term male baby born by uncomplicated pregnancy was brought due to acute onset seizures which terminated with IV lorazepam. He was exclusively breast fed since birth. Examination was unremarkable. His electrolytes test showed low magnesium (0.3 mmol/l) and calcium levels (1.51 mmol/l)which required multiple IV calcium and magnesium replacement initially. Blood pH was normal. Vitamin D level were low (21 nmol/l), high PTH level (31 pmol/l), Ca: Creatinine <0.9. Maternal Vitamin D and Magnesium levels were (10 nmol/l and 0.63 mmol/l). Both mum and child received oral Calcium, Vitamin D and Magnesium supplementation on discharge. Although the calcium levels normalised on follow ups, the infant's magnesium levels remained subnormal even with high doses of oral magnesium supplementation. His development was up to date at the time of his recent 8 month follow up.
Discussion
Vitamin D deficiency continues to be a problem in developed countries. Maternal vitamin D deficiency is one of the major risk factors for early infantile vitamin D

deficiency followed by hypomagnesemia due to infantile hypocalcaemia. It was of interest to note that in our patient, therapy with calcium as well as with magnesium resulted in clinical improvement and caused elevation of serum calcium but not rise in magnesium levels. He remains under follow up with Endocrine team and further plan is to carry out urinary magnesium studies and genetic testing to rule out familial hypomagnesemia.
Conclusion
Our case illustrates the importance of checking both calcium and magnesium levels in early infants who presents with seizures. It is worthwhile to check both child and maternal vitamin D status in infantile hypocalcemia as this is an easily correctable condition. Persisting hypomagnesemia in this infant warrants further evaluation to rule out familial hypomagnesemia.

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Diabetes 1

P17

Management of type 1 diabetes and HbA1c audit

Khine Wut Yee Kyaw, Allison Grove & Victoria Hemming
Mid Yorkshire Teaching NHS Trust, Wakefield, UK

Background
There is clear evidence that achieving optimal glycaemic control in type 1diabetes reduces the complications of diabetes. Increased technology use is associated with lower HbA1c. NICE target HbA1c is 48 mmol/mmol.
Objective
Are there differences in HbA1c between patients with Type 1 diabetes using continuous glucose monitoring sensor (CGM) or hybrid closed loops in real world setting in paediatric patients at Mid Yorkshire Teaching NHS Trust?
Method
Compare the most recent HbA1c in September 2022 with HbA1c from 2021 for 313 of patients with Type 1 diabetes aged 0–18 years under the MY Paediatric diabetes service.
Results
57% of patients were on injections, 21% on pump and 22% on pump with closed loop. For glucose monitoring, 55% use CGM, 37% Libre and 7% use finger prick glucose testing. We found that HbA1c improved with CGM across all age groups (by up to 10%). The biggest reduction in HbA1c was seen in groups using injections with CGM and those with using hybrid closed loop system.
Conclusion
CGM and hybrid closed loop systems improve HbA1c. Following updates to local commissioning policy in line with NICE guidance on use of CGM all children and young people under the care of MY Paediatric Diabetes service will be encouraged to use CGM. We await the NICE Technology Appraisal on hybrid closed loop systems.
HbA1c improvement after using continuous glucose monitoring

	Mean HbA1c (mmol/mmol)			
Age (yr)	Baseline	End-point	Difference	Improvement
<5	81.86	62.29	19.57	23.91%
5–9	71.08	58.76	12.32	17.33%
10–14	74.68	63.58	11.10	14.86%
15–19	72.58	67.02	5.56	7.66%
Total	73.24	64.02	9.23	12.60%

Median HbA1c difference among different groups

	Baseline	End-point	Difference	Improvement
Group 1 – Insulin Injection	62	65	−3	−4.03%
Group 2 – Injection + libre	69	65	4	5.11%
Group 3 – Injection + CGMS	71	64	7	9.22%
Group 4 – Pump + Libre	64	60	4	6.30%
Group 5 – Pump + CGMS (without Closed-Loop)	60	56	4	6.67%
Closed-Loop	62	57	5	8.06%

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P18

Acceptability of a general population childhood type 1 diabetes screening programme: a qualitative study – T1 Early

Claire Scudder[1], Julia Townson[2], Jane Bowen-Morris[2], Philip Evans[3], Sarah Jones[4], Nick Thomas[4], Jane Stanford[5], Robin Fox[5], John Todd[1], Sheila Greenfield[6], Kathleen Gillespie[7], Colin Dayan[1,2] & Rachel Besser[1]
[1]University of Oxford, Oxford, UK. [2]Cardiff University, Cardiff, UK. [3]University of Exeter, Exeter, UK. [4]Windrush Medical Practice, Witney, UK. [5]Bicester Health Centre, Bicester, UK. [6]University of Birmingham, Birmingham, UK. [7]University of Bristol, Bristol, UK

Background
General population screening for type 1 diabetes (T1D) using islet autoantibodies (IAb) is gaining international momentum, since screening reduces diabetic ketoacidosis, hospitalisation and identifies individuals eligible for future preventative treatments. Qualitative studies have only been undertaken in at-risk individuals (1). We therefore aimed to explore parents' experiences of their child taking part in a general population T1D screening programme.
Methods
Children attending their pre-school vaccination at age 3.5–5 years ($n=63$) provided a capillary sample for IAb testing. We undertook semi-structured interviews with parents, after their child's participation in screening, and before receiving the test result. These methods allowed us to get in-depth opinions from people with first-hand experience. We also provided postcards to collect open question feedback to participating parents and those that declined to take part. Data were analysed thematically, using NVivo 12.
Results
Qualitative interviews: 15 parents undertook semi-structured interviews. Participants were uniformly positive about screening aligning to the vaccination programme, citing that they may have been less likely to take part had screening been a separate visit. Themes identified included being prepared in the event of a T1D diagnosis, feeling reassured by a negative test result, and the long-term benefit of screening outweighing short-term upset. Parents reported that the volume of blood was higher, and collection time longer, than expected. Postcard data 32 postcards were received, 29 from participants, and 3 from parents who declined. Themes identified were broadly similar to the interviews. Participants who declined all went ahead with vaccinations. Two parents cited not wanting to engender a fear of doctors as a reason for declining.
Conclusions
To our knowledge, this is the first time qualitative methodologies have been used to understand the experience of general population T1D screening, as part of a routine health visit. This approach may enable more widespread uptake and could be cost saving. When aligned to routine vaccination, the experience of childhood T1D screening was uniformly positive, however blood collection methods need development before future rollout.
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P19

Improved glycaemic control with insulin hybrid closed-loop system

Shien Chen Lee, Katie Brown, Susan Muniu & Kathryn Mccrea
Princess Royal Hospital, Telford, UK

Introduction
Hybrid closed-loop system (HCS) in Type 1 diabetes (T1D) management uses an automated algorithm to adjust basal insulin and administer correction doses to maintain glucose homeostasis. We have more children with HbA1c <58 mmol/mol. We aim to investigate if HCS contributed to this improvement.
Methods
We identified TID children who started on HCS in our hospital from the year 2019–2023. Our HCS are Medtronic continuous glucose monitoring (CGM) with Medtronic 670G and 780G pumps and Dexcom CGM with T-slim and DANA pumps. The start date of HCS was recorded. Mean HbA1c was analysed for the year before and the year after starting HCS. The results were compared to see if our patients' glycaemic control improved. Statistical significance was determined using paired t-test. Data was obtained using our electronic patient record.
Results
102 children commenced on HCS within our study period. We excluded 6 children due to insufficient data. Data was collected for 96 children (55% male, 45% female). The median age was 12.4 years. The mean HbA1c pre-HCS was 61 mmol/mol and this significantly improved to a mean HbA1c of 56 mmol/mol after HCS ($P<0.0000004$). 21 patients with a mean HbA1c of more than 69 mmol/mol had an impressive reduction of an average 15 mmol/mol post HCS

($P<0.00005$). For the remaining patients, mean HbA1c improved from 57 mmol/mol to 54 mmol/mol post-HCS ($P<0.0006$). Children on multiple daily injections had higher mean HbA1c (62.8 mmol/mol) pre-HCS when compared to those on insulin pumps (60.8 mmol/mol). Both groups achieved similar mean in HbA1c in the year after HCS (55.8 mmol/mol). The number of children with HbA1c less than 58 mmol/mol increased from 37 to 55 children. 32 patients have HbA1c values at 2 years. More than half of them maintained HbA1c of <58 mmol/mol. Limitations to our study include short follow-up and variable HbA1c measurements due to the Covid pandemic and non-clinic attendances.
Conclusion
There is significant improvement in our patients' glycaemic control since the use of HCS. Although greater progress was seen in those with poorer metabolic control, a longer follow-up is needed in this patient group to see if these outcomes are sustained.

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P20

Abstract withdrawn

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P21

Don't forget bone health: Increased fracture risk in type 1 diabetes

Rebecca Moon[1,2], Elizabeth Curtis[1], Stefania D'Angelo[1], Zahra Raisi-Estabragh[3], Cyrus Cooper[1,4,5] & Nicholas Harvey[1,4]
[1]MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK; [2]Paediatric Endocrinology, University Hospital Southampton NHS Foundation Trust, Southampton, UK; [3]William Harvey Research Institute, NIHR Barts Biomedical Research Centre, Queen Mary University of London, London, UK; [4]NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital NHS Foundation Trust, Southampton, UK; [5]NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK

Objectives
Fracture risk is increased in individuals with diabetes mellitus, but how this is related to bone mineral density (BMD), adiposity, inflammation, disease duration and diabetic complications is less well understood. We aimed to investigate associations between type 1 (T1DM) and type 2 (T2DM) diabetes and incident fracture in a large population study.
Methods
UK Biobank is a population study incorporating individuals aged 40–69 years recruited during 2006–2010 from across the UK. A baseline assessment included detailed review of demographics, lifestyle, medical history, anthropometry, blood sampling and in a subset, bone mineral density (BMD) assessment by quantitative ultrasonography. We used Poisson regression to calculate incidence rate ratios (IRRs) for fracture to investigate a) prospective relationships between diabetes and fracture risk (ascertained from self-report and/or hospital records, mean follow-up time 12.3 years (S.D. 1.9)) independent of traditional clinical risk factors for fracture [BMD, fat mass and inflammation (C-reactive protein)]; b) the impact of microvascular complications; c) interaction with duration of diabetes.
Results
There were 498 949 participants (45.5% male, mean age 56.5 years). 1836 (0.4%) had T1DM and 20 551 (4.1%) had T2DM. Fracture risk in T1DM was increased, independent of BMD, fat mass and CRP, compared to no diabetes (IRR 2.75 (95%CI 2.25, 3.36)) and T2DM (IRR 1.23 (95%CI 1.12, 1.34). Associations were similar by sex. Younger age at diagnosis of T1DM conferred mildly higher fracture risk (diagnosis at 0–10 years IRR 3.10 (95%CI 1.64,5.85), 10–20 years: IRR 2.92 (95%CI 1.99,4.27), 20–30 years: IRR 2.68 (95%CI 1.93, 3.73), 30–40 years: 2.07 (95%CI 1.34,3.22)). In individuals with T1DM, the presence of any microvascular complication conferred an increased fracture risk (IRR 1.72 (95%CI 1.15, 2.57), with a dose effect by number of complications. The risk associated with neuropathy (IRR 2.62 (95%CI 1.56,4.38)) or nephropathy (IRR 2.16 (95%CI 1.24,3.77)) was greater than eye disease (1.63 (95% CI 1.08,2.45)) in T1DM, with similar findings in T2DM.
Conclusions
Fracture risk is increased in adults with T1DM, independent of BMD, adiposity and inflammation. This risk is increased further with younger age at diagnosis and microvascular complications. Advice on optimising skeletal health should be part of diabetes care.

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P22

Exploring the social and clinical impact of a residential activity camp for children and families with type 1 diabetes: A video-based study of camp Charnwood

Steve Green[1] & Dr Victoria Dublon[2]
[1]Royal Free Hospital Childrens' School, London, UK; [2]Royal Free Hospital, London, UK

Aim
Promoting cohesion, community and knowledge of diabetes through the co-production of a video exploring the social and clinical impact of attending a residential activity camp for children and families living with type 1 diabetes
Method
From our knowledge of attending previous diabetes camps, the video will begin by highlighting the background and motivation behind the study, emphasising the limited understanding of the social and clinical benefits of a residential activity camp spanning over 5 days. With full consent, will be filming the 2023 camp between July 25th and July 30th and fully edited and completed well before the September deadline. Our goal will be to bridge this gap and shed light on the potential positive impacts diabetes camps can have on the lives of those attending. The video will show how we gathered the information from interviews, observations and activities. We will share glimpses of the camp setting, from the grounds of Beaumanor Hall in Leicestershire, showcasing the supportive environment, interactions with medical staff and camp helpers (most of whom attended the camp when younger), and the engaging activities on offer such as canoeing, high ropes, orienteering and archery to name a few. The video will illustrate the social benefits of fostering a community, expressing what it means to them, including enhanced peer support, reduced feelings of isolation, an increased sense of normalisation and improved self-esteem and self-efficacy. Additionally, we will highlight instances of any clinical outcomes observed, such as greater awareness of time in range and a general increase in knowledge and confidence of Diabetes Self-Management Education. We will endeavour to capture the personal stories allowing viewers to witness the transformative impact the camp has on daily lives. In particular, we will capture the strengthened inter and intra family bonds forged during the camp experience.
Conclusion
Residential camps play an important role in fostering psychosocial well-being and improved health outcomes for children and families. This co-produced video will enable conference attendees and members of the diabetes community to experience camp at a deeper level, promoting attendance and awareness of the benefits of residential diabetes camps.

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P23

Atrial natriuretic peptide and copeptin levelsrelationship with serum osmolality in pediatric patients with diabetic ketoacidosis

Seyda Karahan, Zerrin Orbak, Busra Demir & Nurinnisa Ozturk
Atatürk University, Erzurum, Turkey

Introduction
Diabetic ketoacidosis is a metabolic event that occurs as a result of the absence or deficiency of insulin and the increase in contrinsuliner hormones, resulting in disruption of electrolyte and water regulation. In this study, it was planned to investigate the changes in ANP, copeptin, renin, aldosterone levels before and after rehydration and insulin therapy in pediatric patients with a diagnosis of diabetic ketoacidosis followed in the pediatric endocrinology clinic, so that the results obtained will shed light on the pathophysiology of diabetic ketoacidosis.
Materials and methods
Our study is a prospective study and we evaluated the serum osmolality, serum sodium and plasma glucose levels and the degree of dehydration, and the dynamic changes of ANP, copeptin, renin and aldosterone levels due to rehydration and insulin therapy in 31 patients who were followed up in our clinic with the diagnosis of diabetic ketoacidosis. The study was supported by the Atatürk University Scientific Research Projects Commission (TTU-2021-9262).

Results
While ANP increased statistically significantly, other parameters were found to decrease statistically significantly after treatment ($P=0.001$). When the correlation between the ANP, copeptin, renin and aldosterone levels of the patients at the time of diabetic ketoacidosis was examined; there was a statistically significant negative correlation between ANP and copeptin, between ANP and renin, and between ANP and aldosterone. In addition, there was a statistically significant positive correlation between copeptin and renin ($P<0.001$). Also, when the patients with diabetic ketoacidosis included in the study were grouped as severe and mild-moderate ketoacidosis according to pH values, it was determined that there was no significant difference between the two groups in terms of serum ANP and copeptin values, but renin and aldosterone values were higher in severe diabetic ketoacidosis.
Conclusion
Copeptin may be a reliable marker of AVP secretion and may replace AVP in measuring circulating AVP levels in clinical routine. Both the renin angiotensin aldosterone system and the vasopressin system are involved in the hemodynamic impairment during diabetic ketoacidosis. Renin aldosterone and copeptin levels are initially elevated in patients with diabetic ketoacidosis. Serum copeptin level and secretion are not driven by serum sodium concentration.

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P24

A UK survey on the screening and management of childhood pre-clinical type 1 diabetes

Rabbi Swaby[1], Tabitha Randell[2], Claire Scudder[1], Jane Bowen-Morris[3], Julia Townson[4], Colin Dayan[1,5], Loredana Marcovecchio[6] & Rachel Besser[1,7]
[1]JDRF/Wellcome Diabetes and Inflammation Laboratory, Wellcome Centre for Human Genetics, University of Oxford, Oxford, UK; [2]Nottingham Children's Hospital, Nottingham University Hospitals NHS Trust, Nottingham, UK; [3]Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, UK; [4]Centre for Trials Research, Cardiff University, Cardiff, UK; [5]Clinical Diabetes and Metabolism, Cardiff University, School of Medicine, Cardiff, UK; [6]Department of Paediatrics, University of Cambridge, Cambridge, UK; [7]NIHR Oxford Biomedical Research Centre, John Radcliffe Hospital, Oxford, UK

Introduction
Type 1 diabetes (T1D) onset may start years prior to clinical presentation. Screening children and young people (CYP) for T1D using islet autoantibodies (IAb) through research studies is gaining international momentum, since screening reduces diabetic ketoacidosis, hospitalisation and offers access to drug therapies for delaying T1D onset[1]. Recently, ISPAD provided recommendations on monitoring for pre-clinical T1D in CYP, however no UK-specific guidelines or clinical care pathways exist[1]. This survey aimed to gather information on clinicians' experience of managing CYP with $\geq$ 1 IAb, who were not on insulin therapy.
Methods
We distributed an online survey through the BSPED newsletter to non-training substantive doctors (Feb-May 2023). Questions related to CYP with positive IAb and their clinical management over the preceding 2–3 years.
Results
There were 47 respondents; 35 responded as individuals, 12 on behalf of their entire unit. Sixteen respondents had been referred 36 CYP with positive IAb; 17 (47%) identified through clinical care, 19 (53%) through a research study. Reported management included a combination of HbA1c testing (27%), education on signs and symptoms of T1D (24%), capillary/venous glucose testing (18%), research study referral (13%), sensor glucose monitoring (11%), and no action (2.2%). Two respondents referred patients to a research study without clinical follow-up. Twenty-nine respondents reported $\sim$200 parental requests for sibling IAb testing, over the preceding 2–3 years. In response, 32% provided reassurance, 52% referred to a research study, and 6% organised IAb testing in clinical care.
Discussion
Increasingly CYP in the UK are being screened for T1D in research studies and clinical care, with high demand for sibling testing, which will likely increase now that teplizumab is licensed in the US[2]. However, the varied responses to referrals highlight the need for a UK consensus on monitoring and follow-up clinical care pathway.
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P25

Evaluating the impact of planned ward admissions in High HbA1c patients

Sijith Radhakrishnan & Taffy Makaya
Oxford Children's Hospital, Oxford, UK

Introduction
NICE guidelines recommend additional support is provided to CYP with a high HbA1c. Elective hospital admissions are one option for improving glycaemic control.
Aims/objectives
To evaluate the implementation of, and impact on HbA1c of, planned admissions in CYP in our service.
Methods
All planned admissions for management of sustained high HbA1c in patients with known T1D from 01/01/2021-31/12/2022 were included for review.
Results
Patient demographic data: Eight patients were identified, three aged 3years, and 5 aged 13–17years. M:F ratio = 6:2. Duration of diabetes was: 8-months to 11-years, average duration of 3-years 2-months. All 8 patients were on subcutaneous injection therapy: $n=7$ on MDI injections; and $n=1$ on Tresiba and Humulin M3. Admission HbA1cs ranged from 71 mmol/mol to >140 mmol/mol.
Inpatient management:
Average inpatient stay was 6 days in $n=8$ (range 3–14 days). Review by the MDT was as follows:
Table 1 Review by MDT members.

Seen by→ Seen on↓	Consultant	PDSN	Paediatric Dietitian	Clinical psychologist
Day 1	25%	100%	37.5%	50%
By Day 3	75%	100%	100%	87.5%

Three patients had inpatient reviews by the social services team. There were no weekend diabetes MDT reviews. HBA1c and therapy outcomes: Two patients were discharged on insulin pump therapy, and $n=6$ had significant adjustments to their subcutaneous insulin dosage regimen. Table 2 shows HbA1c outcomes from admission upto 12-months post-admission.
Table 2 HbA1c outcomes.

	HbaA1c post admission (mmol/mol)			
Patient Number	**0-months (Baseline)**	**0–3 months**	**3–6 months**	**6–12 months**
Patient 1	133	66 ↓	76↑	58 ↓
Patient 2	117	46↓	54↑	66 ↑
Patient 3	109	87↓	104↑	104 ↔
Patient 4	93	78↓	89↑	86 ↔
Patient 5	71	63↓	57↓	n/a
Patient 6	>140	72↓	72↔	73 ↔
Patient 7	81	65↓	66↔	68 ↔
Patient 8	116	112↓	101↓	89 ↓
Average HbA1c	**107.5**	**73.63 ↓**	**77.38↔**	**77.71 ↔**
pValue		***0–3-months: 0.013***	***0–6 months: 0.017***	***0–12 months: 0.019***
Ave-HbA1c Delta				

Discussion/conclusion
Planned admissions are useful in managing high HbA1cs, resulting in clinically and statistically significant improvements in HbA1c (>5 mmol/mol/ pValue < 0.05). Overall improvement was sustained at 12 months, despite some rebound in HbA1c. Having a clear plan for the admission is helpful in organising MDT staff resources.

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P26

Lipoprotein Lipase (LPL) gene mutation in a girl with diabetic ketoacidosis, acute pancreatitis and hypertriglyceridemia

Duygu Düzcan Kilimci[1], Alkan Bal[1], Ferda Özkınay[2] & Betül Ersoy[1]

[1]Manisa Celal Bayar University, Faculty of Medicine, Manisa, Turkey; [2]Ege University, Faculty of Medicine, İzmir, Turkey

The combination of acute pancreatitis (AP), severe hypertriglyceridemia (HTG), and diabetic ketoacidosis (DKA) possess a life-threatening triad. The pathogenesis of HTG is explained by insulin deficiency, but although DKA is a frequent complication in children and adolescents, this triad is rare. We report a 10-year-old girl with Type 1 Diabetes Mellitus (DM) for 10 months, who presented with DKA, severe HTG and AP. Her serum was lipemic. She had HTG (1733 mg/dL) and severe abdominal pain that did not improve despite treatment for ketoacidosis. She had high serum lipase concentration (1581 U/L) and serum amylase concentration 1581 U/L, and stage E pancreatitis were detected on abdominal tomography. The patient, whose very low-density lipoprotein (VLDL) level was high during the attack, did not have dyslipidemia either before or after the attack. She recovered with a combination of hydration and insulin therapy. A heterozygous p.N318S (c.953A > G) variant was detected in her lipoprotein lipase (LPL) gene. Additionally, her apolipoprotein B (ApoB) was elevated at 1.44 g/L. It is well established that both the likely pathogenic LPL variants and high ApoB concentrations contribute to increased risk of cardiovascular complications. LPL gene mutation should be considered in severe HTG and/or AP detected during DKA in children and adolescents with T1DM even if they have no history of dyslipidemia. Detection of these mutations may also be important in predicting long-term cardiovascular risks.

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P27

Type 1 diabetes associated with primary sclerosing cholangitis and inflammatory bowel disease – a rare autoimmune combination

Shilpa Shah[1], Sarinda Millar[1], Girish Gupte[2] & Louise McLaughlin[3]
[1]Southern Health and Social Care Trust, Craigavon, UK; [2]Birmingham Childrens Hospital Liver Unit, Birmingham, UK; [3]Belfast Health and Social Care Trust, Belfast, UK

Introduction
Type 1 diabetes is an autoimmune condition resulting in insulin deficiency. Surveillance of other autoimmune disorders such as coeliac disease and hypothyroidism is common practice due to their higher co association. We describe a case of a 14 year old girl with 2 rarer autoimmune conditions; primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD)
Case summary
A 14 year old girl presented with abdominal pain, weight loss and tiredness for a few weeks. She had no history of polyuria or polydipsia, jaundice, diarrhoea or vomiting. On examination she had no hepatomegaly. Her blood tests revealed a moderate elevation of liver enzymes. Her liver ultrasound was normal. A month later she was diagnosed with type 1 diabetes. Her liver functions remained elevated therefore was referred to the regional liver unit. Further investigations confirmed a diagnosis of PSC. She was started on ursodeoxycholic acid with improvement in liver functions. Her diabetes was managed initially through multiple daily injections and thereafter by patch pump. She maintained excellent time in range. She was then actively screened for IBD. Her faecal calprotectin was very elevated. She then underwent biopsies which confirmed a diagnosis of IBD. She was started on medications for the same. In a space of 6 months she was diagnosed with 3 chronic conditions all managed by different specialists. 2 years on she remains in good health with normal liver functions, excellent time in range on ambulatory glucose profile and improving faecal calprotectin.
Discussion
Conditions like IBD and PSC can co exist albeit not routinely screened for in type 1 diabetes due to their extremely low prevalence rates. Our patient presented with raised liver function tests prior to her diabetes symptoms and therefore was diagnosed with PSC independently rather than through screening. Once a diagnosis of PCS was confirmed she was screened for IBD through faecal calprotectin due to reported prevalence rates of IBD up to 80% in patients with PSC. This presentation does not make a case for routine screening of liver functions testing in new diagnosis of type 1 diabetes but could be considered if abdominal symptoms remain unexplained.

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P28

Enhancing engagement in a diabetes camp for families and young people: A promising approach to empowerment and sustainability during a cost of living crisis

Steve Green[1] & Dr Victoria Dublon[2]
[1]Royal Free Hospital Childrens' School, London, UK; [2]Royal Free Hospital, London, UK

Aim
Camps offer valuable opportunities for creating a supportive environment of like-minded people with similar experiences of living with diabetes, thereby promoting self-efficacy, wellbeing and a healthy life style. In the midst of a post-Covid cost of living crisis, finance was identified as a major obstacle for families wishing to attend residential diabetes camps. A sustainable strategy, supported by co-production with young people, was needed to facilitate access to Camp Charnwood in Leicestershire.
Method
Almost £6000 was raised through a sponsored London to Brighton cycle ride. The camp was then heavily promoted at diagnosis and during clinic visits. In order to establish the strengths, weaknesses, opportunities and threats of reintroducing an established diabetes camp after lockdown, children, parents and helpers were surveyed as part of a (Plan-Do-Study-Act) PDSA cycle to increase participation for future camps.
Results
- Attendance increased from 1 to 7 families from our Trust compared to the previous year
- Enough money was raised to provide transport
- The activities were tailored to consider the suggestions polled in the questionnaire. For example, a more inclusive, wheelchair friendly terrain for the 5-mile walk, separate activities for older children, a parallel programme for parents providing opportunities to share ideas, good practice and more time to meet with the attending Diabetes Doctor and Specialist Diabetes Nurse, and avoiding the large queues at Alton Towers by staying with Drayton Manor
- The PDSA cycle will continue and data added to the final poster/presentation as camp runs again this July

Conclusion
Fundraising and promotion increased participation from our Trust for the 2023 camp, and will continue. Children demonstrated improved knowledge, self-efficacy and overall well-being as evidenced by their participation, fun and enthusiasm in camp activities. Children without diabetes were also overheard to use diabetes related language such as 'hypos', 'time in range' and 'I keep getting alerts from someone running high' for the first time. This was good for normalisation. Moreover, the camp provided a nurturing environment fostering empathy, shared experiences, friendship and emotional support, boosting both parental and child engagement and a positive sense of belonging where everybody 'just gets it'.

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Diabetes 2

P29

Introduction of under-fives type 1 diabetes clinic improves glycaemic control through rapid access to automated insulin delivery systems

Chamila Balagamage, John Pemberton, Louise Collins & Ruth Krone
Department of Endocrine and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK

Introduction
Achieving glycaemic targets for young children with type 1 diabetes (T1D) is challenging due to rapidly changing physiology and behavioural patterns. An under-fives specialised multidisciplinary clinic (U5-MDT) was implemented in January 2022 due to poorer glycaemic control in this group compared to the rest of the clinic cohort. The U5-MDT aimed to optimise glycaemic control through access to technology while providing family support.
Methodology
Evaluation of all children under five years with T1D who had been diagnosed at least one year (out of honeymoon) before their first U5-MDT. Descriptive data was collected and reported by percentage or mean ($\pm$ standard deviation) on socioeconomic status (SES, 1–5 quintiles, 1 = most deprived), age at diagnosis, gender, duration of diabetes at final reporting, interpreter required, and diabetes therapy from the electronic patient record system. We compared one month of glycaemic control a year after diagnosis to the glycaemic control for one month using their latest download (collected July 2023), which was at least six months after the first U5-MDT by paired t-test (two-tailed, $P < 0.05$). Outcome measures were time below range (< 3.9 mmol/L), time in range (3.9 – 10.0 mmol/L), and time above range (> 10.0 mmol/L).
Results
12 children (five male) mean age at diagnosis of 2.3 years ($\pm$1.5) with a T1D duration of 2.5 years ($\pm$1.2) at final data collection were evaluated. A quarter of families required an interpreter, and 75.0% (national average 23.7%) were from the most deprived SES quintile. All children used continuous glucose monitoring

before the U5-MDT clinic started, with only two using an automated insulin delivery system (AID). By July 2023, 10 of 12 were using an AID. Before U5-MDT vs. after U5-MDT, the change outcome measures were; TBR 2.8% (±1.9) vs. 2.5% (±1.2) [0.3% (95% CI −0.9 to 1.5), $P=0.3$], TIR 41.6% (±17.8) vs. 58.8% (±12.3) [−17.3% (95% CI −30.8 to −3.7), $P<0.05$], TAR 55.5% (±12.3) vs. 37.1% (±13.4) [18.3% (95% CI 4.0 to 32.7), $P<0.05$].
Conclusion
A dedicated U5-MDT allows better support and quicker access to AID, improving glycaemic outcomes. Hence, we suggest initiating targeted under-fives clinic prioritising technology and support.

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P30

Type 1 diabetes in pre-school children: Identifying targets for quality improvement through a countywide review evaluating clinical presentation, management, and outcomes

Jessica Dale
Worcestershire Acute Hospitals NHS Trust, Worcester, UK

Introduction
Pre-school children with Type 1 Diabetes are a vulnerable group of patients, presenting both diagnostic and management challenges which can place them at increased risk of worse glycaemic control and the complications of Diabetes. The use of advancing diabetes-related technologies including continuous glucose monitoring (CGM) and Hybrid-closed loop (HCL) systems offers the real potential to improve outcomes.
Aim
To conduct a countywide review of pre-school children newly diagnosed with Type 1 Diabetes, evaluating clinical presentation, management and outcomes including HbA1c.
Method
Children aged 0–4-years and newly diagnosed with Type 1 Diabetes between 1st April 2020 and 1st January 2023 were identified using the countywide Diabetes patient database. Clinical notes were retrospectively reviewed.
Results
Twenty-two children aged between nine months and four years eight months were identified. Seventeen (77.3%) children presented in DKA, with seven (41.2%) classified as severe; six (35.3%) moderate and four (23.5%) mild. Preceding diagnosis, eight children (36.4%) had either attempted to, or had seen a healthcare professional, increasing to 41.1% amongst those presenting in DKA. Once commenced on subcutaneous insulin, it took a mean of 41.86 (S.D. 59.35) days for children to start using insulin to carbohydrate ratios and only seven (31.8%) started within fourteen days. All patients had been commenced on a CGM device (flash or real-time), with the average time to CGM improving significantly between 2020–21 and 2021–22, although there still exists a delay. Thirteen (59.1%) children had commenced pump therapy, taking a mean of 429.38 days from diagnosis. This cohort demonstrated an improvement in mean HbA1c from 97.12 mmol/mol (seventeen patients) at diagnosis to 67 mmol/mol (fourteen patients) at twelve months. However, this improvement of 30.12 mmol/mol (95% CI 17.64–42.6, $P=0.0001$) remains sub-optimal.
Conclusion
This review identifies the need for enhanced education and awareness of the risk of T1D in pre-school children after three-quarters presented with Diabetic Ketoacidosis (DKA). Results also indicate that outcomes are sub-optimal and pump therapy is being under-utilised in this patient group. Early introduction of HCL systems should be considered.

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P31

Abstract withdrawn

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P32

A new educational tool for prevention of DKA at diagnosis of type 1 diabetes

Michael McGuigan[1], Philippa Bowen[2], Carol Metcalfe[3], Nicky Moor[4], Marlon Morais[5,6], Charlotte Rowland[7,8], Ambika Shetty[9], Tamsyn Nicole[10], Jonathan Maiden[11], Emma Savage[12] & Margot Carson[11]
[1]Countess of Chester Hospitals NHS Foundation Trust, Chester, UK; [2]Bristol Royal Hospital for Children, Bristol, UK; [3]Royal Manchester Children's Hospital, Manchester, UK; [4]Barts Health NHS Trust, London, UK; [5]Ashton Medical Group, Ashton-Under-Lyne, UK; [6]NHS Greater Manchester ICB, Manchester, UK; [7]Handbridge Medical Centre, Chester, UK; [8]Cheshire and Merseyside ICB, Cheshire and Merseyside, UK; [9]Children's Hospital for Wales, Cardiff, UK; [10]Yeovil District Hospital, Yeovil, UK; [11]Children and Young People's North West Diabetes Network, Leeds, UK; [12]Children and Young People's Yorkshire and Humber Diabetes Network, Leeds, UK

Late diagnosis of type 1 diabetes, leading to diabetic ketoacidosis (DKA) is a significant concern in the UK. The National Paediatric Diabetes Audit 2021/22 showed that 25.6% of children and young people diagnosed with type 1 diabetes in England and Wales presented in DKA, with a rising trend over recent years. Reduction in DKA at diagnosis is part of Aim 1 of the National Children & Young People's Diabetes Network (NCYPDN) Delivery Plan 2020–25. A working group was created including diabetes healthcare professionals, GPs and representation from Diabetes UK. The group intends to support regional diabetes networks in understanding their own DKA data, and putting local strategies into place to achieve DKA reduction. As part of this work the group are creating educational resources that can be used to promote best practice in recognition of type 1 diabetes in children by healthcare professionals. One project is creating a slide set that can be used by an educator to deliver a 20 minute talk at a local primary care education event. However, there was also felt to be a need for a shorter tool that could be used for self-directed e-learning by GPs and nurse practitioners. A short educational tool was therefore developed that can be shared with primary care health professionals electronically. The consists of a short slideshow that is designed to be opened and read by the user on their own computer, and takes around 5 minutes to complete. The tool gives a short background on the importance of reducing DKA at diagnosis, explains the correct pathway for responding to symptoms, discusses human factors that may affect diagnosis, and gives some case examples to support the learning points. Feedback on the tool was gathered from diabetes and primary care healthcare professionals in the North West. A final version is planned to be launched on the NCYPDN website in September 2023: www.cypdiabetesnetwork.nhs.uk/national-network/dka-prevention-at-diagnosis/

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P33

Neonatal diabetes: A challenging case scenario and therapeutic considerations

Sathesh Kumar Sajithbhavan Kuttappan[1], Stuart Davision[1] & Shaju Edavana[2]
[1]North Devon District Hospital, Barnstaple, UK. [2]University Hospital of North Midlands, Stoke on Trent, UK

Neonatal Diabetes
A Challenging Case Scenario and Therapeutic Considerations Neonatal diabetes is a rare form of diabetes mellitus that presents in the first six months of life. This abstract highlights a challenging case scenario of neonatal diabetes and provides insights into the diagnostic approach, therapeutic considerations, and long-term management strategies. The case involves a term male neonate who presented with severe hyperglycemia, polyuria, and failure to thrive. Initial investigations revealed persistently elevated blood glucose levels, and further evaluation led to a diagnosis of neonatal diabetes. Genetic testing identified a novel mutation in the KCNJ11 gene, confirming the diagnosis of permanent neonatal diabetes. The therapeutic management of this case required a multidisciplinary approach, involving pediatric endocrinologists, geneticists, and intensive care specialists. Insulin therapy was initiated promptly to achieve glycemic control, and careful monitoring of blood glucose levels and nutritional intake was implemented. Genetic counseling was provided to the parents, elucidating the autosomal dominant inheritance pattern of the KCNJ11 mutation and its implications for future family planning. Long-term management involved regular follow-up visits to assess growth, development, and glycemic control oral hypoglycemic drug of glbenclamide,Adjustment of insulin doses was carried and later able to stop. The importance of diabetes education and support for the family was emphasized to facilitate adherence to treatment and optimize outcomes. This case scenario

highlights the complex nature of neonatal diabetes and the significance of early diagnosis and appropriate management. It also highlights the unique feature of response to oral hypoglycemic agent.Genetic testing played a crucial role in confirming the diagnosis and guiding treatment decisions. Multidisciplinary collaboration and ongoing patient monitoring are essential for achieving optimal glycemic control and minimizing the risk of long-term complications. In conclusion, this case scenario underscores the challenges encountered in the diagnosis and management of neonatal diabetes. It emphasizes the importance of a comprehensive approach involving genetic testing, individualized therapy, and long-term follow-up to optimize the care and outcomes of infants with this rare condition.

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P34

Effect of the T-Slim pump with control IQ hybrid closed loop system on physiological and psychological outcomes in children with type 1 diabetes in gloucestershire

Lottie Till, Victoria Cullen & Mihirani Balapatabendi
Gloucestershire Hospitals NHS Foundation Trust, Cheltenham, UK

Background
In March 2022, NICE guidelines advised that real-time continuous glucose monitoring (rtCGM) be offered to all children and young people with type 1 diabetes mellitus (T1DM). Using rtCGM alongside the hybrid closed loop system (HCLS), has transformed management of T1DM in adults and children alike by linking insulin delivery to sensor glucose levels.
Aim
To evaluate how the T-Slim pump with control IQ HCLS affects both clinical parameters and quality of life in children/their parent(s) within a group of 11 paediatric patients with T1DM aged 8–16 in Gloucestershire.
Methods
Clinical parameter data was collected retrospectively from rtCGM system (Dexcom G6). Clinical parameters assessed were time in range, % time spent in hypoglycaemia, % time spent in hyperglycaemia, HbA1c and mean glucose. Quality of life data was collected using a quality of life scoring sheet. Scores were calculated using parent interview answers. Areas measured included problems with symptoms, problems with treatment, worries, communication regarding illness with family/friends/healthcare professionals and parental opinions. For both clinical parameters and quality of life, data was collected before, at 6 months and at 1 year.
Results
Participants ranged from 8 to 16 years, 45.5% female. Patients were under the Gloucestershire Royal Hospital paediatric diabetes team and had had a diagnosis of T1DM for between 3.1 and 13.8 years. At study end point, there was an overall improvement in all clinical parameters – 4.6% absolute % increase in median TIR, 2.13% absolute % decrease in median mean glucose, 1.6% absolute % decrease in median time spent in hypoglycaemia, 9.6% absolute % decrease in median % time in hyperglycaemia, 6.15% absolute % decrease in HbA1c. There was also a 24.5% improvement in quality of life. However, mean glucose and time in range values were better at 6 months than at 1 year.
Conclusion
The T-slim pump with control IQ HCLS was associated with improvement in both clinical parameters and quality of life, in our patients with T1DM.

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P35

Use of sensor augmented pump therapy is safe and effective in patients with significant deprivation and high risk HBA1c

Janet Soo, Angeline McCabe, Paula Smith & Chris Gardner
East Lancashire Hospitals NHS Trust, Blackburn, UK

Background
Advances in insulin pumps and continuous monitoring mean that, where indicated sensor augmented pump therapy (SAPT) can be prescribed for children under NHS care in England. National Paediatric Diabetes Audit (NPDA) data shows improved diabetes outcomes (in terms of HBA1c) in children managing their diabetes in this way. Use of this technology is significantly lower in children in the lower deprivation quintiles and in patients from non white ethnicity, both whom have higher HBA1c. It is uncertain whether the outcomes seen in the NPDA are due to the technology or to other social and educational factors.
Design
As a unit with significant deprivation (48% patients are in quintile 1) and high levels of patients of non white ethnicity (28%), East Lancashire was awarded funding to improve the uptake of technology. Families were invited to a technology roadshow. Subject to meeting NICE criteria, patients were offered a choice of 3 pumps – Omnipod + Dexcom G6 (non SAPT at time of pump start), T Slim with Control IQ (SAPT) and Yposmed pump with CAMAPS (SAPT). Full training and follow up were provided for all patients. Outcomes including time in range, and episodes of diabetic ketoacidosis were tracked pre and post intervention.
Results
31 Patents were commenced on pump therapy:

Pump	No of patients	Pre HBA1c	Average Deprivation Decile	Time in range (TIR) 1 month pre	TIR 1 month post	TIR 2 months post
Omnipod	15	66	5	46	42	47
T Slim	5	72	4	43	65	63
CAMAPS	11	64	3.4	45	60	65

11 patients had HBA1c > 69 mmol/mol pre pump. Average HBA1c in this group fell from 82.1 mmol/mol pre to 62.71 mmol/mol post. For those on sensor augmented pump therapy in this group the reduction was from 81 mmol/mol to 60.4 mmol/mol. One patient discontinued pump therapy however there were no episodes of DKA.
Conclusion
SAPT resulted in improvements in time in range in patients from deprived and non white backgrounds with high HBA1c compared with non SAPT technology. In this group it was safe and effective. SAPT should be considered as an option in these patients and actively offered.

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Examining the relationship between social deprivation, health outcomes and technology uptake in a district general hospital setting – are we providing equity in our service?

Lucy Austreng & Edward Coxson
Royal United Hospital, Bath, UK

Introduction
The International Diabetes Federation 2019 Diabetes Atlas states that the UK has the highest number of children and young people aged 0–14 with Type 1 Diabetes in Europe, with the incidence of cases observed to be rising on a national and international level. The National Paediatric Diabetes Audit (NPDA) 2020–2021 report identified countrywide inequalities between measures of diabetic health and treatment devices used within the paediatric diabetes population, including higher HbA1c measurements in those living in deprived areas, and children living in the least deprived areas being more likely to be access real-time capillary glucose monitoring. These disparities must be addressed to ensure the medical optimisation of every paediatric diabetes patient, regardless of their background.
Aim/objective
This project aimed to review the data and outcomes for our local Paediatric Diabetes Unit (PDU) and identify any similar inequalities in the management of our patient group.
Methods
All paediatric diabetes patients were classed by their Index of Multiple Deprivation (IMD) result, obtained via their postcodes. Various indicators of treatment were reviewed including HbA1c, completion of all Key Care Processes (KCPs), admissions with diabetes-related complications, and the monitoring and treatment devices they were using.

Results
Analysis is evolving, but current results suggest that within our patient population, there were a higher proportion of children completing 100% of KCPs in the highest IMD quintile and a higher rate of hospital re-admissions with diabetes-related complications in the middle quintile, where the lower IMD quintiles were excluded due to a small number of patients within those groups. The median HbA1c was highest in the lowest IMD quintile, with the trend broadly decreasing as the IMD quintile rises. There were generally a higher proportion of children in lower IMDs whose families were receiving additional social support.
Conclusions
Initial data analysis suggests there may be a correlation between a lower IMD and markers of poorer diabetes control and complications within our own paediatric diabetes unit. This data will be used to drive quality improvement and identify new ways to support children and their families within our service.

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P39

Right diagnosis, right treatment: Think MODY early in children who present with symptoms of diabetes

Alagusutha Jeyaraman, Mohamed Khair & Rumbidzai S Jhamba
Hull Royal Infirmary, Hull, UK

Background
Although it accounts for small number (1–2%) of diabetes cases, MODY is especially important to be picked up by health care providers because of the implications of the correct diagnosis on clinical management and family counselling. MODY should be suspected when a patient <25 years old presents with symptoms of diabetes, who has a family history of diabetes/ MODY, with negative diabetes autoantibodies screen, and/or suboptimal response to insulin.
Case 1
A 15year old girl who was diagnosed of diabetes after presenting with classical diabetes symptoms with hyperglycaemia and positive family history of diabetes not in acidosis and was started on basal insulin. Diabetes related antibodies were negative. On follow up, HbA1c remained <48 mmol/L, and there was no response to insulin therapy with high blood glucose around 20 mmol/L but low ketones. Urinary C-peptide 7.83 nmol/l She scored 7.2% on MODY calculator and monogenic diabetes genetic test was positive for the HNF1A mutation. Glycaemic control improved on replacing insulin with gliclazide.
Case 2
an 8 years old boy who was referred to us from outpatient clinic because of an incidental finding of an HBA1C of 53. There was strong positive family history of MODY on the maternal side. His mum had the glucokinase mutation. 2 of his maternal uncles aged 28 and 14 years also had a confirmed diagnosis of MODY. The genetics results for this patient are still pending.
Conclusion
MODY is a rare and yet the commonest form of monogenic diabetes. It is characterised by onset before 25 years, absence of β-cell autoimmunity and sustained pancreatic beta cell function. So, patients with MODY do not usually have diabetic ketoacidosis (DKA). It has autosomal dominant pattern of inheritance so there is often a family history of diabetes and there is a 50% risk of the offspring to have the condition. Early treatment decreases the risk of micro and macrovascular complications of diabetes, so early detection and appropriate management are paramount to sustain quality of life of the affected children when they enter adulthood.

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Gonadal, DSD and Reproduction 1

P40

Systematic review and meta-analysis of spermatogenesis rates after pubertal induction with gonadotropins in males with hypogonadotropic hypogonadism

Emma Alexander[1], Kyla Ng Yin[1], Duaa Faruqi[2], Robert Farquhar[2], Ayesha Unadkat[2], Rachel Varughese[1] & Sasha Howard[1]
[1]Queen Mary University of London, London, UK. [2]Barts and The London School of Medicine and Dentistry, London, UK

Background
Hypogonadotropic hypogonadism is characterised by inadequate secretion of gonadotropins (luteinising hormone (LH) and follicle-stimulating hormone (FSH)) leading to absent, partial or arrested puberty. In males, classical treatment with testosterone promotes virilisation but does not facilitate testicular growth or spermatogenesis. Conversely, treatment with gonadotropins stimulates Sertoli and Leydig cells directly, leading to increased testicular volumes, testosterone concentrations, and spermatogenesis. We sought to systematically review studies of gonadotropins for the induction of spermatogenesis in males with hypogonadotropic hypogonadism.
Methods
Systematic review of studies since 1990 of patients with hypogonadotropic hypogonadism treated with gonadotropins for 6+ months, across Medline, EMBASE, Global Health, and PsychInfo databases, in December 2022. RoB 2.0/ROBINS-I/NHLBI scoring for quality appraisal. Protocol registered on PROSPERO (CRD42022381713).
Results
After screening 3925 abstracts, 106 studies were identified (81 observational studies, 19 comparative non-randomised studies, six randomised controlled trials), including 5377 patients from 21 countries. Of these, 98 evaluated spermatogenesis. Median NIHLBI score for observational studies was 9/12 (interquartile range (IQR) 8–10) and 44.0% of comparative studies had serious risk of bias in at least one domain. The average age of participants was <25 years in 45.3% ($n=48$) of studies. Studies utilised hCG ($n=96$, 90.6% of studies), hMG ($n=44$, 41.5%), FSH ($n=38$, 35.8%), and 28.3% ($n=30$) used GnRH. Median reported duration of treatment/follow-up was 18 months (IQR 11.5–24 months). Meta-analysis of proportions found a pooled proportion of patients achieving spermatogenesis with a random effects model was 38.9% for hCG (95% CI 24.5–54.1%), 85.7% for hCG + FSH (95% CI 81.1%–89.8%), 73.7% for hCG + hMG (95% CI 65.3–81.4%) and 72.1% for GnRH (95% CI 58.9–83.9%). There was substantial heterogeneity for all treatment modalities except hCG + FSH, where there was moderate heterogeneity. The most frequent adverse effects were gynaecomastia, acne and injection site pain/reaction.
Conclusions
There is increasingly promising evidence regarding the use of gonadotropins to induce spermatogenesis in males with hypogonadotropic hypogonadism. We found that hCG + FSH was superior to hCG alone for induction of spermatogenesis. However, there remains substantial heterogeneity in study design and therapeutic regimens, and randomised studies are needed to inform guideline development for this important cohort.

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P41

A retrospective analysis of clinical characteristics, testosterone therapy, and comorbidity screening for klinefelter syndrome: Insights from a UK tertiary centre over the last two decades

Dhivyalakshmi Jeevarathnam, Manju Chandwani, Abhijit Dixit & Pooja Sachdev
Queen's Medical Centre, Nottingham, UK

The European Academy of Andrology (EAA) recently published consensus guidelines aiming to standardize the care provided to patients with Klinefelter syndrome (KS) across different stages of development. In this retrospective cross-sectional study, we reviewed the clinical care provided to 76 KS patients at Nottingham University Hospitals between 2000 and 2020.
Methods
Data regarding age at presentation ($n=30$ paediatric, adult 46), presenting complaints, treatment and screening for co-morbidities were collected.
Results
- The mean age at KS diagnosis was 25.8 ± 15.5 years.
- The most common presenting symptoms were developmental delay and behavioural disorders in the under-five (40%), 6–10 years (67%), and 11–18 years (35%). Absence of secondary sexual characteristics was a leading complaint in 25% aged 11–18 years and 4% of adults.

- Sexual dysfunction (33%), infertility (57%), and gynecomastia (31%) were the chief symptoms observed in adults. Urological symptoms, bone health issues, and easy fatigability were less common.

Testosterone therapy

- The mean age at initiation of testosterone was 29.45 ± 16.05 years.
- At the time of diagnosis, the mean levels of FSH, LH, and testosterone were 29.3 ± 19 IU/L, 14 ± 10 IU/L, and 6.3 ± 4.5 nmol/L, respectively.
- The choice of preparation at initiation depended on the availability (gel in 33%)
- Adverse effects included male pattern baldness, nausea, leg cramps, and mood swings.
- Two patients had elevated PSA levels, and one was diagnosed with prostatic carcinoma.

Follow-up

- Regular endocrine follow-up was noted in 45%.
- Multidisciplinary team (MDT) assessment was provided to 50% of patients (100% in the 6–10 years)
- Community paediatricians saw 33% of the cohort.
- Amongst the adults, 21% were discharged from endocrinology to primary care.

Comorbidity screening

- 50% of paediatric patients were screened for hypothyroidism.
- 56% of adult men were screened for metabolic complications, 22% had a lipid profile, 44% were screened for bone health, and 80% had thyroid function tests.
- Only 11% of the study population underwent cardiac evaluation at the time of diagnosis.

Our study results corroborate the under-diagnosis and under-treatment of KS and its related morbidities and substantiate the EAA guidance recommendation for establishing standard care for KS children and adults in multidisciplinary networks.

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P42

Establishing diagnoses in a cohort of boys from East London with 46XY DSD and severe hypospadias

Shahrukh Aamir*[1,2], Christos Papaioannou*[1,2], Ruth Kwong[1,3], Ashwini Joshi[4], Devesh Misra[4] & Rathi Prasad[1,3]
[1]Department of Paediatric Endocrinology, Royal London Children's Hospital, Barts Health NHS Trust, London, UK; [2]Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [3]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [4]Department of Paediatric Urology, Royal London Children's Hospital, Barts Health NHS Trust, London, UK

An underlying genetic/endocrine cause for severe hypospadias is found in up to 20% of affected boys as described in the literature, with environmental and epigenetic factors also believed to play a role. We conducted a retrospective analysis of 65 boys with severe hypospadias (penoscrotal, scrotal, perineal) managed by Paediatric Urology at Barts Health NHS Trust, born between January 2010 and 2021 (38% white caucasian, 28% asian, 22% black and 12% other/undefined). Boys with hypospadias with microphallus and/or cryptorchidism had a significantly lower gestational age as compared to hypospadias alone (median 32.6 Weeks vs 38 weeks; $P < 0.05$). A significantly lower birthweight SDS was seen in boys with hypospadias with both cryptorchidism and microphallus as compared to hypospadias alone (median −2.36SDS vs −1.24 SDS; $P < 0.05$). 38 patients had a one stage and 23, a two-stage surgical repair, with complications described in 45% and 56% respectively, including urethral fistula and requirement for urethral dilatation. When cryptorchidism and/or microphallus were described there was a greater likelihood of referral to endocrinology (82% of individuals with additional features as compared to 12% referred with hypospadias alone, 22 referred in total). The diagnostic yield following biochemical/genetic testing was 14%. Genetic testing undertaken beyond karyotyping included the NHSE R146 DSD 35 gene panel and in those with additional clinical features, a microarray. Whilst 6% of boys had a positive family history of hypospadias, none went on to have an established diagnosis. DSD secondary to 17-hydroxylase deficiency (urine steroid profile and confirmed genetically), VACTERL association secondary to compound heterozygous variants in *TRAP1* (100 000 genome project), and a heterozygous *NR5A1* variant (DSD gene panel) were diagnosed in 3 boys, born at term with normal birthweight and normal inhibin B results. 3 further patients had low inhibin B (< 60 pg/mL), all with a history of IUGR, 2 with cryptorchidism and microphallus (diagnoses to be determined). Diagnostic yield is low for affected boys however there is growing consensus that even those with isolated severe hypospadias warrant further investigation. Importantly, when established, diagnoses allowed for appropriate management of associated comorbidities and genetic counselling. *denotes equal contribution

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P43

Long-term psychosocial and functional outcomes after genitoplasty in virilising congenital adrenal hyperplasia

Arianna Mariotto, Supul Hennayake, Tamas Cserni, Indi Banerjee, Gail Busby, Mars Skae, Leena Patel, Raja Padidela, Philip Murray, Jacqueline Nicholson, Julie Jones, Charlotte Richmond & Anju Goyal
Manchester University NHS Foundation Trust, Manchester, UK

Introduction

Timing of DSD surgery is debated. This study aimed to investigate outcomes of genitoplasty in CAH and assess patient's opinion on surgery.

Materials and methods

In this ethically approved prospective study, surgically treated CAH girls ≥16 years completed an electronic questionnaire.

Results

27 patients were contacted 13 completed questionnaires, 10 declined, 4 did not reply. Current median age 27 (16–48) years and median age at surgery 18.3 (5.7–183.6) months. All identified themselves as female and were comfortable with assigned gender. Six are heterosexual, 3 homosexual, 3 bisexual, 1 unknown. 10 had been in a relationship. Following surgery, 6 had concerns about genitalia appearance and felt that it had negatively impacted formation of sexual relationships. Five reported poor self-esteem. Regarding the choice made for surgery, one was unhappy about having had surgery; 3 were not sure, 5 sometimes questioned that choice. When asked if they would have liked a different decision in terms of timing of surgery, 2 answered yes, 1 was not sure, 10 were satisfied with the decision taken by their parents. Nine disagreed with proposal to stop early surgery, whilst 2 were not sure and 2 agreed.

Conclusion

46XX CAH girls identify themselves as females and are comfortable in their assigned gender. Following surgery, 46% have residual concerns regarding genital appearance, experienced complications including uncomfortable clitoral sensation on erection and felt this adversely affected sexual relationships. 77% of patients were satisfied with parental decision for early surgery. 69% wanted to retain choice for early surgery. More data are needed to support these preliminary results.

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P44

Novel association of NUP107 variants in XY DSD

Shaju Edavana[1], Viba Yadav[2], Anurag Bajpai[3] & Afia Andrews[4]
[1]Royal Stoke University Hospital, Stoke On Trent, UK; [2]Department of Pediatric Endocrinology, Kanpur, India; [3]Department of Pediatric Endocrinology, Regency Center for Diabetes, Endocrinology& Research, Kanpur, India; [4]Birmingham Children Hospital, Birmingham, UK

XY disorders of sexual development (DSD) are rare causes of primary amenorrhea and are associated with significant diagnostic and therapeutic implications. We report a novel association of compound heterozygous missense NUP107 variants in a girl with hypergonadotropic hypogonadism and XY karyotype. This 17-year-old girl born of consanguineous marriage presented with absent breast development and primary amenorrhea. Her past medical history included the surgical removal of an abdominal mass which was histologically confirmed to be a germinoma. There were no features of

chronic illness, neurological involvement, anosmia, hearing difficulty, or hypothyroidism and no family history of delayed puberty. There were no inguinal swellings, and she was normotensive. There were no phenotypic features suggestive of Turner syndrome and no dysmorphisms. She was tall (164 cm; 1.03 SDS; Corrected height SDS +2.2), with normal weight (53 kg, 0.23 SDS) and BMI (19.7 kg/m^2, −0.3SDS) and prepubertal with Tanner staging B1P1. Endocrine investigations revealed hypergonadotropic hypogonadism; LH 44.36 IU/L(RR: 0.5–41.7 IU/L) and FSH 105.6 IU/L (RR: 1.6–17 IU/L)] with undetectable estradiol and testosterone levels. Ultrasound of the pelvis showed a small uterus, and right ovary (1×3 cm), with a non-visualized left ovary. Clinical exome sequencing identified compound heterozygous NUP107 gene missense variants in exons 2 and 4. NUP107, a nucleoporin involved in the cytoplasmic-nuclear exchange, is crucial for cell division and meiotic stability, and its defects have been reported in 46XX girls with hypergonadotropic hypogonadism and ovarian dysgenesis. Diseases associated with NUP107 include Ovarian Dysgenesis 6 and Nephrotic Syndrome, Type 11. Functional experiments have shown a gender-selective reproductive phenotype of NUP107 defects without impacting male fertility. Integration of genetic sequencing in cases of 46 XY DSD are warranted to aid diagnosis. Early diagnosis is essential so that HRT treatment begins at the appropriate time as well as counselling about the associated higher risk of malignancy and infertility. A specialist multidisciplinary approach with regular follow-up is required. This is the first report of NUP107 variants in the setting of XY DSD, highlighting the need to elucidate the role of this gene in male reproductive development.

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P45

17β-HSD3 deficiency: A single centre experience

Khubaib Ahmed[1] & Talat Mushtaq[2]
[1]Leeds Children's Hospital, Leeds, UK; [2]Leeds Children's Hospital, Leeds, UK

17 β-Hydroxysteroid Dehydrogenase Type 3 (17β-HSD3) deficiency is an autosomal recessive condition causing 46, XY disorder of sexual development (DSD). The enzyme is responsible for converting of Δ4-Androstenedione (A) to testosterone (T) in testicles. Affected individuals may present with abnormalities of the external genitalia at birth or during childhood and teenage years with virilisation or primary amenorrhea. The aim of this case series is to review the clinical, biochemical and genetics characteristics of individuals diagnosed with 17β-HSD3 deficiency in a single tertiary centre. 4 cases were identified between 2010 and 2023 All had karyotype 46, XY. One presented at birth with palpable gonads, one at age 8 with clitoromegaly and two at age 16 with primary amenorrhea. A summary of the characteristics is presented below: All patients received multidisciplinary input from paediatric endocrinology, genetics, psychology and surgery. Apart from the one diagnosed in infancy all continued to live as females and commenced GnRH analogues and oestrogen. Three of the children had minimal increase in the testosterone following HCG injection with T/A ratio of less than 0.3. 17BHSD is a rare condition that may present in several different ways. The

	Presentation	USS	Post HCG stimulation	Mutation	Outcome
Case 1 16 years	Primary amenorrhea.	No Mullerian structures. Inguinal Testes	T 3.58→3.98 A15.3→16.7 T/A: 0.23	Homozygous splice-site c.277+4A>T	–Female – Decapeptyl and oestrogen –Gonadectomy (malignancy risk)
Case 2 8 years	Clitoromegaly	no Mullerian structures. Inguinal Testes	T: 0.3→1.4 A: N/A T/A: N/A	Heterozygous c.614T>A p.(val205Glu) and C.645A>T p.(Glu215ASP).	– Female – oestrogen – Gonadectomy
Case 3 3 days	Normal female external genitalia and palpable gonads groins.	no Mullerian structures. Inguinal Testes	T: 0.6→1.5 A:10.9→18.9 T/A: 0.08	homozygous mutation C.210delA, p(lys70fs)	–Male –Testosterone IM – Orchiopexy and reconstructive surgeries.
Case 4 16 years	Primary amenorrhea.	no mullerian structures. Abdominal Testes on MRI	T: 4.2→7.2 A:11.8→34.1 T/A: 0.21	–	–Female – Decapeptyl – Oestrogen

complexity of the condition requires extensive discussion with patients/family and MDT approach for management.

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P46

X-Chromosome genomic alteration leading to primary ovarian insufficiency in an adolescent: A case study

Manju Chandwani, Neeta Lakhani, Emily Craft & Savitha Shenoy
Leicester Royal Infirmary, Leicester, UK

Recent advancements in genetic testing have revealed various X-chromosome abnormalities as causative factors for both familial and sporadic cases of Primary Ovarian Insufficiency (POI). In this case report, we present an intriguing instance of POI associated with a deletion in the critical region-1 on the long arm of the X-chromosome A 12.5-year-old girl of South Asian descent presented with 8 month history of irregular menstrual periods with bleeding lasting for 10 days and a cycle length of approximately 24 days. She had attained menarche at the age of 9 and there was no notable past medical history or fertility issues in her family members. Examination revealed her weight to be 62.6 kg (98th percentile), height 157.5 cm (75th percentile), and BMI 25.2 kg/m^2. She was in well-established puberty and had no dysmorphic features, hirsutism, or acanthosis nigricans. Investigations were in keeping with POI (FSH – 54 IU/L, LH – 20 IU/L, 17-Beta Oestradiol < 70 pmol/L). Ultrasound examination showed a normally developed uterus measuring 38 mm in length but with a very thin endometrium. Both ovaries had a volume of 5.9 cc, but no developing follicles. Ovarian antibodies were not detected. Other investigations (Prolactin, TSH, 17-OHP, Coeliac screen) were all normal. AMH was low at <0.2 pmol/L. Array comparative genomic hybridization (array CGH) revealed two X-linked copy number variants 46, X, der(X)(pter->q27.2::p21.1->pter) – arr[hg19]Xp22.33p21.1x3, Xq27.2q28x1. The patient exhibited duplicated genetic material (31.3 Mb terminal gain) on the short arm and a 13.4 Mb terminal deletion on the long arm of one of her X chromosomes. This abnormality was not identified on array CGH of either of patient's parents. Our patient does not fit the classification of Turner syndrome due to the absence of Xp monosomy. She has a deletion within the critical region-1 (Xq26-q28, POI 1) on one of her X-chromosomes and this is likely to be a significant contributing factor to her POI. The deleted region encompasses 248 genes, many of which are considered crucial for normal ovarian function, however our understanding of the precise mechanism by which this region contributes to POI remains limited.

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P47

A rare cause of gonadal dysgenesis due to TOE1 gene mutation

Mohsina Noor ibrahim, Meherunnisa Yasir, Yasirnaqi Khan, Saadullah Chachar, Roshia Parveen, Maira Riaz & Versha Rai
NICH, Karachi, Pakistan

Introduction
46XY gonadal dysgenesis is one of the important cause of DSD with varied clinical presentation Genetic mutations like SRY, NR5A1, SOX9, DHX37 are common mutations that can cause gonadal dysgenesis. Genetic testing for reaching final diagnosis in 46 XY DSD is increasingly playing a crucial role in the management plan.
Case
A 10-month-old patient presented in our DSD clinic with complaint of atypical genitalia which were noticed at birth. The child was a product of consanguineous marriage. Initial rearing was female but at 2 months of age the sex of rearing was changed to male. There was no history of virilization or maternal drug intake during pregnancy. The child was developmentally normal with no abnormal findings. Anthropometric parameters were normal. On genital examination the genitalia were asymmetrical and EMS score was 4. The patient had micropenis, right gonad was absent and left was present in the inguinal region.On ultrasound the right gonad (0.3×0.5 cm) was present peritoneally and left gonad was present in the mid-inguinal region (0.6×0.3 cm). Karyotype was 46XY with satellites on chromosome 15 and 22. AMH was low and testosterone levels initially normal. On HCG stimulation there was a blunted response with normal stimulated T/DHT ratio. Mullerian duct remnants was demonstrated in genitogram. MRI brain was normal.Genetic panel for 46XY DSD

(53genes) was sent. It revealed homozygous mutation of TOE1 gene c.480G>C (p.Lys160Asn variant). This gene is extremely rare and very few cases have been reported. Laparoscopy and surgery has been planned.

Discussion

Mutation in TOE1(Target of early growth response gene 1) leads to defects in DNA replication. Other diseases associated with Pontocerebellar Hypoplasia Type 7 and Familial Adenomatous Polyposis 2.Various human phenotypes of TOE1 mutations are seen in both 46XX and 46XY leading to abnormalities of genitalia. Conclusion:. In largely consanguinous married population of Pakistan diverse genetic disorders are quite common. Very rare mutations have also been reported in 46XY DSD. TOE 1 gene has been reported for the first time in 46XY DSD from Pakistan.TOE1 gene should be included in genetic panels of 46 XY and XX DSD.

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P48

Navigating complexity: Long-term follow-up of an 18-year-old patient from Pakistan with 45 X0 and SRY activating mutation: Ambiguous genitalia, rearing challenges, and pubertal induction

Roshia Parveen[1], Versha RAI[2], Professor Mohsina Noor Ibrahim[2] & Maira Riaz[2]
[1]Pediatric Endocrine Department, National Institute of Child Health, Karachi, Pakistan; [2]National Institute of Child Health, Karachi, Pakistan

We present a case study of an 18-year-old child from Pakistan with a complex medical history and a prolonged follow-up period. The patient initially presented at 5 months of age with ambiguous genitalia, leading to a male gender assignment. However, subsequent investigations, including karyotyping, revealed a 45 X0 chromosomal makeup. Additional imaging studies, such as pelvic ultrasound and genitogram, unveiled the presence of ovaries, uterus, and a testicular structure in the inguinal region. Following these findings, the patient's gender was re-assigned to female at the age of 5 months. However, shortly after this re-assignment, the patient was lost to follow-up. Remarkably, the patient returned for further evaluation at the age of 9 years. Comprehensive investigations, including fluorescence *in situ* hybridization (FISH) and SRY gene analysis, were conducted, revealing the presence of the SRY gene in 19% of 500 nuclei tested. The left gonad was identified in the left inguinal region, prompting laparoscopy and biopsy procedures. Biopsy results indicated the presence of a vas deferens structure in the left gonad, while the right gonad exhibited ovarian stroma. Consequently, the left gonad was surgically removed. The patient has since been closely monitored and received pubertal induction therapy, despite compromised height. Notably, the patient has successfully achieved puberty under medication. This case highlights the complexities surrounding the diagnosis and management of individuals with intersex conditions and chromosomal anomalies. The unique combination of a 45 X0 karyotype and an SRY activating mutation adds further complexity to the clinical presentation. Long-term follow-up and multidisciplinary care involving endocrinologists, geneticists, and psychologists are essential in addressing the physical, psychological, and social aspects of these patients' development. Continued research and understanding of intersex conditions are crucial to providing appropriate medical interventions, including early diagnosis, gender assignment, and tailored treatments for pubertal induction. Additionally, comprehensive counseling and support for the patients and their families are crucial to ensure holistic care and optimized outcomes in these complex cases.

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P49

Mayer–Rokitansky–Küster-Hauser (MRKH) syndrome – two cases presenting to a large UK Paediatric Endocrinology Centre

Dinendra Siriwardhane[1], Reena Perchard[1,2] & Philip Murray[1,2]
[1]Royal Manchester Children's Hospital, Manchester, UK; [2]University of Manchester, Manchester, UK

The Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome is characterized by congenital absence or underdevelopment of the uterus and upper two thirds of the vagina in females with karyotype XX, alongside normal external genitalia. The prevalence is 1 in 4000 to 5000. It can be divided into two major categories. Type 1 occurs in isolation whilst type 2 involves other organ systems, particularly the renal, vertebral, auditory and cardiac systems. Whilst sporadic in nature, the familial tendency raises the possibility of a genetic aetiology. Here, we report two unrelated cases of MRKH syndrome who are currently under the endocrine follow up at Royal Manchester Children's Hospital. Case 1 is a 22 month old female who was born at 40 weeks' gestation weighing 3.2 kg. She was found to have an imperforate anus at birth and cystoscopy demonstrated an absent vaginal opening. Ultrasound scan showed no müllerian structures nor ovaries. Laparoscopy revealed a hemiuterus and a fallopian tube, with normal ovarian appearances on each side. The karyotype was 46 XX, but disorder of sex development gene panel identified no pathogenic mutations. Investigations showed a serum oestradiol of <3 pmol/L at 4 weeks of age, luteinizing hormone (LH) of 0.3 U/L and follicle stimulating hormone (FSH) of 6.9 U/L at 9 months of age, anti mullerian hormone (AMH) of <0.2 pmol/L and inhibin B <9.8 pg/mL. Urology input is ongoing as a crucial part of the multi-disciplinary team management. Case 2 is a 4 year old female who was born at 38 weeks' gestation weighing 2.06 kg. At birth, an anteriorly placed anus, an appropriately placed urethral meatus and a vagina and a faecal fistula in the vaginal vestibule were identified. Neither a uterus nor a vagina could be identified on the ultrasound or magnetic resonance scan. Renal ultrasound scan was normal but echocardiogram showed pulmonary valve stenosis. Her blood investigations showed an oestradiol of <10 pmol/L, LH 0.6 U/L, FSH 26.2 U/L, AMH 0.34 pmol/L and Inhibin B <9.8 pg/mL at 6 months of age. She is awaiting audiology assessment, due to concerns related to hearing.

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P50

A rare disease of Kallmann syndrome: First case report from Pakistan

Maira Riaz[1], Noshaba Noor[2], Versha Rani[1] & Mohsina Ibrahim[2]
[1]National Institute of Child Health, Karachi, Pakistan; [2]National Institue of Child Health, Karachi, Pakistan

Introduction

First described in 1944, the condition is a rare pediatric genetic disease estimated to affect 1 in 48 000 individuals. Kallmann syndrome is an uncommon hereditary disorder and is among the most frequent cause of isolated congenital hypogonadotropic hypogonadism (CHH). In its classical form, it is characterized by hypogonadotropic hypogonadism and anosmia/hyposmia. Absent endogenous GnRH-induced LH pulsations occur due to failure of neuronal migration of the luteinizing hormone-releasing hormone (LHRH)-secreting neurons and the neurons of the vomeronasal nerve.

Case report

We report a case of a 15-year-old female teenager who presented to the endocrinology department for evaluation of delayed puberty. On further elicitation of medical history, she complained of anosmia, and on examination, no other significant past medical or surgical history was noted. On further inquiry, her maternal grandfather was a color blind.

Investigations

Evaluation of hypogonadism with a hormonal assay of FSH, LH, and testosterone, along with a GnRH stimulation test, revealed their serum concentrations to be below the normal limits; LH 0.20 mIU/mL (normal range: 1.7–15.0) and FSH = 1.08 mIU/L (normal range: 1.9–11.6 mIU/L). With these biochemical investigations, keeping the diagnosis of KS in view, further workup was initiated and an MRI brain with contrast was suggested to look for olfactory tracts in particular and rule out any intracranial pathology.

Radiological findings

MRI brain with contrast revealed the absence of an olfactory bulb in the anterior cranial fossa and olfactory sulcus. The gyrus rectus and medial orbital gyrus formed a single gyrus. These findings were best appreciated on T2W coronal images. Imaging findings were typical for Kallmann's syndrome. The rest of the brain was unremarkable, with no other abnormalities detected. With the relevant clinical picture, biochemical investigations showing low gonadotropic hormonal assays, and MR imaging features of absent olfactory tracts and hypoplastic olfactory sulcus, the diagnosis of KS was confirmed.

Genetics

Genetic workup was sent which suggested FGFR1 mutation (heterozygous variant). It is reported as the culpable mutation for kallmann syndrome with autosomal dominant transmission. The patient was treated with conjugated estrogens for hypogonadism.

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Late effects of cancer treatment

P51

Glucagon-like peptide-1 (GLP-1) receptor agonists as a new treatment option for hypothalamic obesity in the paediatric population: Preliminary data from a tertiary paediatric endocrine centre

Katherine Hawton[1,2], Sumana Chatterjee[1], Dinesh Giri[1,2] & Elizabeth Crowne[1]
[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]University of Bristol, Bristol, UK

Background
Hypothalamic obesity (HO) is defined as rapid weight gain, hyperphagia and lack of satiety due to physical hypothalamic destruction. HO does not usually respond to lifestyle modification and no pharmacotherapies are specifically approved for treating HO. Efficacy of glucagon-like peptide-1 (GLP-1) agonists, which suppress appetite via hypothalamic satiety centres, is uncertain in HO.
Case series
We commenced seven patients (3 female; aged 13–19 years) with HO secondary to suprasellar tumours (3 craniopharyngioma, 3 germinoma, 1 Rathke's cyst) on GLP-1 agonists (liraglutide or semaglutide). At treatment initiation, mean BMI was 37.4 kg/m^2 ($\pm$3.0) with mean BMI-SDS 3.38 ($\pm$0.3). Complications of excess weight included 2/6 with obstructive sleep apnoea requiring overnight ventilation, 1/6 with type 2 diabetes mellitus and 1/6 with non-alcoholic fatty liver disease.
Case 1 commenced on liraglutide (3 mg daily) aged 13.4 years and lost 3.2% bodyweight (BMI–SDS reduction 0.14) after 3 months, which continued at 6 months (8.3% weight loss; 0.44 BMI SDS-reduction) and 12 months (11.8% weight loss; $-$0.63 BMI–SDS reduction).
Case 2 commenced on liraglutide (3 mg daily) aged 16.2 years and lost 4.1% bodyweight (BMI–SDS reduction 0.24) after 3 months, which continued at 6 months (7.0% weight loss; 0.41 BMI SDS-reduction) and 12 months (8.6% weight loss; 0.63 BMI–SDS reduction).
Case 3 commenced on semaglutide (2 mg weekly) aged 13.8 years, after continued weight gain on liraglutide, and weight stabilised with 0.61% weight gain (0.32 BMI–SDS reduction) over 12 months.
Case 4 commenced semaglutide (1 mg weekly) aged 18.9 years, lost 2.79% bodyweight (BMI–SDS reduction 0.18) after 3 months and 1.86% weight loss (0.18 BMI SDS-reduction) at 6 months.
Encouraged by these results, three further patients recently commenced semaglutide therapy but auxological follow-up data is awaited, including one patient who was unsuccessfully established on liraglutide therapy due to nausea. All six patients reported increased satiety and less pre-occupation with food.
Conclusion
Our initial results demonstrating response to GLP-1 therapy in HO are promising. More longer-term data are required to evaluate its use for treating HO and associated sequelae. Weight stabilisation, rather than loss, may also be considered to reflect a successful treatment outcome in this challenging patient cohort.

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P52

Abstract withdrawn

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P53

Precocious puberty and other endocrine disorders during mitotane treatment for pediatric adrenocortical carcinoma – cases series

Elżbieta Moszczyńska[1], Marta Baszyńska-Wilk[1], Aleksandra Tutka[1], Agnieszka Bogusz-Wójcik[1], Patrycja Dasiewicz[1], Małgorzata Walewska-Wolf[2], Maria Stepaniuk[3], Wiesława Grajkowska[3], Dorota Majak[4] & Olga Gryniewicz-Kwiatkowska[5]
[1]Department of Endocrinology and Diabetology, The Children's Memorial Health Institute, Warsaw, Poland; [2]Gynecological Outpatient Clinic The Children's Memorial Health Institute, Warsaw, Poland; [3]Department of Pathology, The Children's Memorial Health Institute, Warsaw, Poland; [4]Department of Diagnostic Imaging, The Children's Memorial Health Institute, Warsaw, Poland; [5]Department of Oncology, The Children's Memorial Health Institute, Warsaw, Poland

Introduction
Adrenocortical carcinoma (ACC) is a rare and aggressive tumor. Mitotane has been the mainstay adjuvant therapy of ACC. The study aimed to describe patients diagnosed with precocious puberty (PP) and other endocrinological disorders during mitotane treatment.
Material and methods
This retrospective study enrolled four children with ACC treated with mitotane complicated by PP. The patients were diagnosed at Children's Memorial Health Institute (CMHI) in Warsaw, Poland. We analyzed clinical manifestations, radiological, histopathological findings, and hormonal results.
Results
The median age at the diagnosis of ACC was 1.5 years (range 0.75 – 7.5 years). The first symptoms of ACC were the appearance of pubic hair and clitoromegaly (in two patients). Children underwent adrenalectomy, and histopathological examination confirmed the diagnosis of ACC. In one patient, a metastatic lesion occurred in the contralateral adrenal gland. All patients were treated with mitotane and, in two children, accompanied by other chemotherapy regimens. The median time from surgery to the initiation of mitotane therapy was 26 days. During mitotane treatment, PP was confirmed based on symptoms, hormonal and imaging tests. The median time from the therapy initiation to the first manifestations of PP was 4 months. In one patient, incomplete peripheral PP was followed by central PP, and gonadotropin-releasing hormone analog (triptorelin) treatment was introduced and continued for 2.5 years. Additionally, due to mitotane-induced adrenal insufficiency, patients required a supraphysiological dose of hydrocortisone (HC), and in one patient, mineralocorticoid (MC) replacement with fludrocortisone was necessary. In two patients, hypothyroidism was diagnosed, and levothyroxine treatment was introduced. Patients presented with neurological adverse events related to mitotane therapy. The following manifestations were observed in our study group: dysarthria, unsteady gait, muscular hypotonia, decreased tendon reflexes, and tremors of limbs.
Conclusions
The side effects of using mitotane should be recognized quickly and adequately treated. In prepubertal children, PP could be a complication of therapy. The need to use supraphysiological doses of HC, sometimes with MC, should be pointed up. Some patients require levothyroxine replacement therapy. In addition to endocrinological side effects, the neurotoxicity of mitotane is a significant clinical problem.

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Miscellaneous / other 1

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Incidence, aetiology and outcome of infants presenting with low sodium and high potassium – population surveillance study in Wales

Rebekah Pryce[1], Shivaram Hegde[1], David Tuthill[1], Tim Cheetham[2] & Yincent Tse[2]
[1]Noah's Ark Children's Hospital for Wales, University Hospital of Wales, Cardiff, UK; [2]Great North Children's Hospital, Newcastle upon Tyne, UK

Background
Infants presenting with life threatening hyponatraemia and hyperkalaemia present a diagnostic conundrum that can reflect abnormally low aldosterone production (e.g. congenital adrenal hyperplasia (CAH), renal resistance to aldosterone associated with infected urinary tract malformations or single gene disorders also associated with failure of the kidney to respond to aldosterone (pseudohypoaldosteronism). Although incidence figures for individual conditions exist, no overall data exists for presentation of this characteristic laboratory pattern and underlying cause.
Method
Population-based surveillance study July 2021 to June 2023. Cases were identified by paediatricians using the monthly electronic Welsh Paediatric Surveillance Unit (WPSU) reporting system. Hospital biochemists and tertiary specialists were recruited to optimise ascertainment. Inclusion criteria were term infants $<$12 months with sodium $<$130 mmol/L ($<$2.5 s.d.) AND Potassium $>$5.5 mmol/L ($>$2.5 s.d.).
Results
13 notifications were reported with two additional cases identified by receiving subspecialists. In total 10 infants over two years met inclusion criteria, resulting in an incidence of 1.7 cases of low sodium and high potassium per 10 000 infants per year. Eventual diagnoses were: 3 CAH, 4 transient pseudohypoaldosteronism (3 with underlying urinary infection and urinary tract malformation), one associated with RSV bronchiolitis, one associated with maternal hyponatraemia, one uncertain. Details of eight cases were available by abstract submission deadline. All were white ethnicity infants with birth weights $>$3 kg. 50% were male. Infants presented at median 14 days old (1 hour to 3 months). 4/7 (57%) were shocked or with $>$10% weight loss. All received 0.9% normal saline fluid boluses

with 1/7 receiving insulin for hyperkalemia. Serum sodium and potassium corrected by median one day after admission (range 0–3 and 0–2 days respectively). Patients were discharged after median 6 days (range 3–17). One infant represented after one week with a seizure with normal neuro-imaging and examination. No other sequelae were reported at one month follow up.
Conclusion
This first ever study of infants presenting with severe hyponatraemia and hyperkalaemia across a whole population confirms that this biochemical picture is rare. Most have either CAH or renal aetiology. Normalisation of biochemistry derangement was rapid, and short-term outcome was favourable.

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P55

Phenotyping hypophosphatasia using UK primary care electronic health records

Orlando Buendia, Hadley Mahon & Ghazanfar Khan
Mendelian Ltd, London, UK

Objectives
Hypophosphatasia (HPP) is a rare genetic disorder. Early diagnosis is challenging due to the disease's complexity and low physician awareness.1 This study aimed to demonstrate how a digital health approach that scans electronic health records (EHR) may lead to earlier diagnosis of HPP.
Methods
Patients with HPP were identified in the Optimum Patient Care Research Database (OPCRD), a UK database of 13.7 million patients' primary care EHR. Cases were identified by the presence of the SNOMED-CT diagnostic code for HPP. The clinical features that make up the diagnostic criteria for HPP were mapped to the appropriate SNOMED-CT codes.1 All EHR with a diagnostic code for HPP were examined for the presence of clinical features of HPP in advance of their diagnostic date. Descriptive statistics of HPP clinical features, categorised by organ system, were performed including EHR count and time before diagnosis. Each clinical feature was summarised by EHR count, mean and median time (months) to diagnosis.
Results
The total number of EHR with an HPP diagnostic code was 201. The total number of EHR with HPP features before diagnostic code with ages between 0 – 18 years old was 61. A total of 22 clinical features suggestive of HPP were identified and categorised into 10 organ systems. The clinical feature with the highest number of EHR unique counts was fractures ($n=15$), with a mean and median time to diagnosis of 280 months and 238 months, respectively. Six clinical features had an EHR count ≥ 5: mouth ulcer (13; [151 mean months], [49 median months]), low alkaline phosphatase (10; [52], [6]), delayed motor milestones (9; [104], [86]), rickets (7; [0], [0]), carious teeths (5; [37], [26]) and seizures (5; [180], [17]). A total of nine clinical features identified had an EHR count of <5.
Conclusions
HPP clinical features can be identified in patients' EHR in advance of diagnosis. The identified clinical features may be used to develop phenotypical prediction tools to help identify patients at risk of HPP. Further work is needed to build an algorithm and validate these results with control comparisons.

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P56

Use of long-acting somatostatin analogue in a paediatric patient with MEN1 – a case report

Jessica Borg Olivier, Christina Wei & Louise Izatt
ELCH, London, UK

Introduction
Multiple endocrine neoplasia type 1(MEN1) is an autosomal dominant disorder resulting from pathogenic variant in tumour suppressor gene MEN1 and is characterized by parathyroid, pancreatic islet and anterior pituitary tumours. We describe an unusual case of MEN1 patient who presented with pancreatic neuroendocrine neoplasms (pNEN) prior to onset of puberty.
Case report
A Caucasian boy with a diagnosis of maternally inherited MEN 1 heterozygous missense (c.547T>C) pathogenic variant entered the surveillance programme from the age of 7. At 10y, he presented with abdominal pain and diarrhoea (later diagnosed as overflow diarrhoea). During his annual fasting (6 hr) blood tests, he was found to have hyperinsulinaemic hypoglycaemia (insulin 132 pmol/L, glucose 2.2 mmol/L). MRI showed 19 mm pancreatic lesion within the tail. Controlled fast confirmed suspicion of asymptomatic hypoglycaemia due to hyperinsulinism (HI) which was treated with bedtime 15 g corn-starch. Gallium Dotatate scan showed 2 Dotatate avid pancreatic lesions in head and body as potential sources of insulin production. Tail and body of pancreas were surgically removed, however, the 2nd smaller insulinoma in the head was not excised to preserve pancreatic function. Histopathology confirmed MEN associated pNEN with diffuse microadenomatosis. Repeat MR 1-year post operatively revealed an interval increase (from 7 mm×9 mm to 11 mm×10 mm) in size of the known partially enhancing pancreatic head lesion. Consensus was reached during Neuroendocrine Tumour (NET) multidisciplinary meeting to start long acting somatostatin analogue, Lanreotide 60 mg subcutaneously 4 weekly. Treatment was well tolerated. MR pancreas was repeated 6 months after starting treatment and lesion remained unchanged in size. In view of this positive response it was decided to continue treatment.
Discussion
Primary hyperparathyroidism is usually the first manifestation of MEN1 in childhood. Insulinomas often present later in adult life and are a rare occurrence in paediatric population. There is no published data on the use and dosage of Lanreotide in paediatric patients with pNEN and guidance for its use is extrapolated from other conditions causing hyperinsulinism. The long-term prognosis of using this treatment for pNEN presenting in childhood is so far unknown. Ongoing systematic data collection for such rare diseases is important to increase knowledge base of these conditions.

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P57

Endocrine complications in paediatric patients with transfusion-dependent thalassaemia

Wan Yee Ko[1], Banu Kaya[2] & Ruben Willemsen[2]
[1]Queen Mary University of London, London, UK; [2]Barts Health NHS Trust, London, UK

Introduction
Endocrine complications are common in patients with thalassaemia major. Currently, there is no literature studying the prevalence of endocrine abnormalities within a British cohort of children with transfusion-dependent thalassaemia. Existing literature is mostly based on Greek and other Mediterranean thalassaemia populations, and variations in local management guidelines may result in different clinical outcomes. This study aimed to audit recommended investigations (2016 UKTS recommendations) and evaluate growth and endocrine function in a local cohort of paediatric transfusion-dependent patients.
Methods
Growth and endocrine function of 38 patients with transfusion-dependent thalassemia aged 1–17 under Barts Health trust were evaluated. The number and proportion of patients who had each endocrine assessment completed were calculated. Data was retrieved from electronic patient records.
Results
7 (19.4%) patients displayed short stature (height SDS < -2). Two out of 8 patients with parental heights documented had significantly shorter heights compared to their mid-parental heights (height SDS – mid-parental height SDS < -2). Only 8 (21.1%) patients had sitting heights documented, however, 7 out of these 8 patients (87.5%) displayed disproportionate truncal shortening (leg length SDS – sitting height SDS > 1). Of those eligible for annual endocrine reviews, 11 (55%) were reviewed in joint haematology–endocrinology clinics in the past year, and 2 (10%) were seen in endocrine clinics. 17 (85%) patients received blood tests to assess endocrine function. Six (23.1%) patients had vitamin D deficiency. Other endocrine abnormalities were uncommon in this patient cohort: 1 patient was diagnosed with impaired glucose tolerance, and 1 patient had self-limiting delayed puberty.
Conclusion
Results of this study suggest that endocrinopathy is rare in this paediatric patient cohort which has access to regular transfusions and chelation. Nevertheless, disproportionate truncal shortening and short stature seem common, which may be related to target height potential. Comprehensive monitoring of growth including parental and sitting height measurements are warranted to identify patients in need of further management. Further research on identifying risk factors contributing to reduced truncal height and its interventions may be beneficial.

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P58

Endocrine presentation of a renal disorder

Emma Hawkes & Uma Kumbattae
Staffordshire Children's Hospital at Royal Stoke, Stoke on Trent, UK

Endocrine presentation of a renal disorder. Baby boy born at full term with Birth weight of 4.3 kg and discharged the next day. Baby initially breastfed but losing weight. Advised combination feeding with expressed breast milk and formula milk. Even after increasing feed volume by health visitor baby losing weight. On Day 28 was admitted to the Children's Assessment Unit following a health visitor referral. Baby had a 2 day history of abdominal discomfort and loose stools but no vomiting. On admission baby looked well, not dehydrated. Examination normal with normal genitalia. Blood test showed hyponatraemia (113 mmol/l) and hyperkalaemia (6.7 mmol/l) and admitted to PICU. Urinary steroid profile and 17OHP obtained and started on antibiotics in view of suspected sepsis. Hydrocortisone with Fludrocortisone commenced for suspected diagnosis of Congenital Adrenal Hyperplasia with IV fluids and hyperkalaemia management. Remained stable, and started gaining weight. 17OHP normal (1.3 nmol/l). Sodium supplements and Fludrocortisone were discontinued and electrolytes remained stable. However, a urine sample grew *E. coli*. Cortisol sample sent before starting Hydrocortisone treatment was insufficient, therefore adrenal insufficiency could not be excluded at this point. Baby discharged with open access, a weaning plan for Hydrocortisone, sick day rules and emergency IM Hydrocortisone training. Short Synacthen test arranged. An ultrasound of the renal system showed Hydronephrosis of the left kidney with dilatation of left ureter. Prophylactic Trimethoprim commenced and MCUG and DMSA arranged. Urinary steroid profile normal with a large peak of cholesterol suggestive of a urinary tract infection. MCUG showed Grade 5 vescicureteric reflux and DMSA showed 12%function on left 88% on right kidney. Baby successfully weaned off Hydrocortisone and Short Synacthen test normal. Gaining weight and no further UTI. This case highlights the importance of checking urine and sending for culture in babies with poor weight gain. Patients presenting with suspected adrenal insufficiency must undergo urinalysis and culture to exclude infections. We advise prioritising samples before starting steroids to avoid critical samples being missed, which will help to avoid dynamic testing later.

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Results from learner's feedback on the use of free, globally accessible CME-accredited e-learning modules in paediatric endocrinology and diabetes

Jan Idkowiak[1,2], Conny van Wijngaard-de Vugt4[3], Yvonne van der Zwan[4], Abdulsalam Abu-Libdeh[5], Evangelia Kalaitzoglou[6], Sten Drop[7], Annemieke M Boot[8] & Sze May Ng[9,10]
[1]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK; [2]Department of Endocrinology and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [3]WV Research, Advice and Management, Rotterdam, Netherlands; [4]Department of Pediatric Endocrinology, Amalia Children's Hospital, Radboud University Medical Center, Nijmegen, Netherlands; [5]Al-Quds University, Makassed Islamic Hospital, Endocrinology Unit, Jerusalem, Palestine; [6]University of Kentucky, Barnstable Brown Diabetes Center, Kentucky, USA; [7]Sophia Children's Hospital, Erasmus MC, Rotterdam, Netherlands; [8]University Medical Center Groningen, University of Groningen, Groningen, Netherlands; [9]University of Liverpool, Women and Children's Health, Liverpool, UK; [10]Edge Hill University and Southport and Ormskirk NHS Trust, Southport, UK

Introduction
The ESPE e-Learning web portal is a free, globally accessible online tool to enhance learning in Paediatric Endocrinology and Diabetes. Since August 2022, the e-learning content includes 30 accredited hours of ESPE/ISPAD e-learning Continuing Medical Education (CME) courses with ten core modules each in Paediatric Endocrinology, Paediatric Endocrinology in Resource Limited Setting (RLS) and Paediatric Diabetes. The CME modules were created by world-leading experts in Paediatric Endocrinology and Diabetes and are typically based on consensus guidelines.
Aims and objectives
To assess learner's demographics and feedback from mandatory surveys after completion of the CME e-learning courses and to identify areas for improvement.
Methods
The survey was created by the ESPE e-learning committee and was mandatory upon completion of each CME module. The survey consists of 14 questions and included learner's professional background and country of residence; feedback on the quality of the learning content, presentation, accessibility, and the anticipated impact on clinical practice was assessed by defined questions with a five-level Likert scale, ranging from strongly agree (positive response; 1) to strongly disagree (negative response; 5). The provision of general feedback was encouraged with an open question.
Results
From August 2022, a total of 155 CME modules were completed, 68 (44%) in Paediatric Endocrinology, 63 (41%) in Paediatric Diabetes and 24 (15%) in RLS modules. There was global participation with most learners practising in Europe (65%), followed by the Americas (14.7%), Asia (12.3%) and Africa (7.7%). 43% of users were medical experts, followed by fellows/residents (21%), medical students and nurses (both 12.9%, respectively); 9.6% of learners practice in resource-limited countries. Overall, the learning content was well received for all modules with regards to accessibility, organisation, level of interest, improvement of individual clinical practice, appropriateness of content for individual learning level and provision of feedback following self-assessment (Likert scale 1–2/5). Some learner's free-text feedback identified some areas of improvement, mainly to reduce text-heavy content and to include interactive case reports.
Summary and conclusion
The ESPE CME-accredited e-learning modules are well received and accessed globally to provide free CME education in Paediatric Endocrinology and Diabetes.

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Obesity 1

P60

Abstract withdrawn

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P61

The use of cardiopulmonary exercise testing (CPET) for assessment and guiding interventions in adolescents with obesity

Thomas Larcombe, Nikki Davis, Tom Meredith & Gary Connett
University Hospital Southampton, Southampton, UK

Introduction
Paediatric obesity is increasing globally. By 2050, obesity is expected to cost the UK NHS £10 billion annually.[1] Physical activity and exercise are recognised interventions to reduce BMI.[2] However, the physiological response to exercise is not understood. Understanding physiological responses in people with obesity (PwO) can inform the prescription of safe rehabilitation exercise programmes. This pilot study explored the feasibility of CPET to assess exercise capacity in PwO.
Methods
Patients >135 cm, >12 years old, <160 kg and willing to perform a maximal exercise test, were recruited from our 'Complications of Excess Weight' clinic. Each performed incremental ramp CPET. Key data (VO^2, HR, RER and Watts) were obtained at rest, anaerobic threshold and peak exercise.
Results
15 patients (75% male, mean age 14.8years, mean BMI 42.8) performed CPET. 93% (14) had at least one comorbidity, most commonly ASD/ADHD (7) or hyperphagia (4). 93% (14) achieved maximum exercise performance. At rest, mean VO^2, HR and RER were 3.2 ± 1.6 mL/min per kg, 103 ± 15 bpm and 0.89 ± 0.12. At anaerobic threshold these increased to 11.9 ± 5.1 mL/min per kg, 150 ± 16 bpm and 0.95 ± 0.09. At peak exercise, they were 15.2 ± 5.2 mL/min per kg, 174 ± 14 bpm and 1.1 ± 0.09. Mean load resistance was 96 ± 37 W at anaerobic threshold and 135 ± 49 W at peak exercise. Compared to healthy adolescents, our mean VO^2 peak values were low (15.2 ± 5.2 mL/min per kg versus 42.6 mL/min per kg).[3] Severe deconditioning was the main reason for reduced exercise capacity. There were no cardiac arrhythmias, episodes of hypoxia or other abnormal events.
Discussion
This pilot study provides evidence that maximal CPET is achievable and provides informative data in adolescent PwO. Testing usefully determines the parameters within which exercise can be safely recommended to help promote physical activity and stimulate weight loss.

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P62

Clinical characteristics and complications of excess weight (CEW) seen in multi-disciplinary tier-3 paediatric weight management services: a two centre experience

Katherine Hawton[1,2], Louise Apperley[3], Jennifer Parkinson[3], Meghan Owens[3], Claire Semple[1], Amy Fitzgerald[1], Shelley Easter[1], Kate Clark[3], Kim Lund[3], Ellie Clarke[3], Dinesh Giri[1,2], Senthil Senniappan[3] & Julian Hamilton-Shield[4]
[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]University of Bristol, Bristol, UK; [3]Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [4]NIHR Biomedical Research Centre (Nutrition), University of Bristol, Bristol, UK

Background
Children and young people living with severe obesity experience wide ranging complications of excess weight (CEW), however their prevalence is not well defined. We have evaluated baseline clinical characteristics and complications in two multi-disciplinary tier-3 paediatric weight management services in different regions of the UK.
Methods
All new patients ($n=185$) aged 2–17 years seen in a 12-month period from March 2022 to February 2023 were included. Baseline demographic data was collected, and patients were screened for a range of CEW. PedsQL-4.0 Generic Core Scales questionnaire was used to assess quality of life (QoL).
Results
The mean age was 13.04 years (range 3.33–17.95) and 50.8% were female. The majority of patients were white British (73.8%) and a significant excess living in the most deprived decile (41.4%). The mean BMI was 36.47 kg/m^2 (+8.37 s.d.) and BMI SDS was +3.54 (+0.70 s.d.). Mean body fat ($n=77$) was 48.6% (+8.44 s.d.). Neurodevelopmental problems were common; 27% had autistic spectrum disorder, 10.3% had attention deficit hyperactivity disorder (with 7.0% having both diagnoses), and 14.1% had learning difficulties. Dyslipidaemia (defined by total cholesterol >5.17 mmol/l, LDL > 3.36 mmol/l, HDL < 1.02 mmol/l or triglycerides >1.5 mmol/l) was the most common (51.6%) complication identified, followed by hypertension (29.7%), evidence of non-alcoholic fatty liver disease on ultrasound (17.8%), obstructive sleep apnoea (9.0%) and idiopathic intracranial hypertension (4.9%). Mean HbA1c was 39.0 mmol/mol (+15.18 s.d.; NR <42). Sixteen (8.6%) patients had type 2 diabetes mellitus, with two cases diagnosed through screening in the CEW clinics. QoL scores were low with a mean child-reported questionnaire ($n=82$) total score of 49.51/100 (+19.19 s.d.) and a mean parent-reported questionnaire ($n=87$) total score of 45.81/100 (+19.35 s.d.). Mean scores from a healthy UK paediatric reference population were 82.25 and 81.12 respectively. Mental health problems were common, with 26.2% and 7.7% having diagnoses of anxiety and depression respectively.
Conclusions
We believe we have demonstrated the significant and profound pathology resulting from severe paediatric obesity, highlighting the clinical necessity for CEW clinics. A rigorous approach to identify and manage these physical and mental health complications at an early stage is essential to improve long-term health outcomes.

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The positive effect of liraglutide treatment on body mass index and metabolic profile in adolescents with obesity

Elham Atiq, Louise Apperley, Jennifer Parkinson & Senthil Senniappan
Department of Endocrinology, Alder Hey Children's Hospital, Liverpool, UK

Introduction
Obesity is a chronic and complex disease which is considered as one of the major health challenges with short- and long-term health consequences. Childhood obesity is defined as having a body mass index (BMI) at or above the 95th percentile for age and gender after two years of age. The glucagon-like peptide-1 (GLP-1) receptor agonist, liraglutide, is proven to promote weight reduction when used at a higher dose of 3.0 mg once daily. This study aims to explore the effects of liraglutide on the metabolic profile of children and young people (CYP) with obesity.
Methods
Clinical data was collected on 20 CYP treated with liraglutide with MDT input from a tier-3 multidisciplinary weight management service. Auxological measurements and metabolic profile were obtained at baseline and 3-months post-liraglutide treatment (mean dose 2.4 mg once daily).
Results
The mean age was 14.58 years (range: 12.1–16.7) and 60% (12/20) of patients were female. Significant reductions were found in BMI (1.49kg/m2; 95%CI 0.65–2.34; $P<0.05$), BMI SDS (0.11; 95%CI 0.04–0.17; $P<0.05$), triglycerides (0.26; 95%CI 0.02–0.50; $P<0.05$), and cholesterol levels (0.29; 95%CI 0.02–0.56; $P<0.05$) [Table 1]. A reduction in HbA1c, AST, ALT, LDL was also observed.
Table 1 Measurements obtained at baseline and 3-months post Liraglutide treatment

Measurement	Baseline mean (s.d.)	3-months mean (s.d.)
BMI kg/m2	44.45 (+6.75)	42.96 (+6.89)*
BMI SDS	3.74 (+0.42)	3.64 (+0.48)*
HbA1c mmol/mol	35.55 (+3.82)	34.25 (+3.29)
Fasting insulin pmol/L	251.82 (+127.70)	252.88 (+135.56)
Fasting c-peptide	1448.59 (+454.33)	1483.24 (+574.48)
AST iu/L	19.84 (+6.22)	18.68 (+4.07)
ALT iu/L	25.63 (+12.58)	25.42 (+11.87)
Triglycerides mmol/L	1.09 (+0.53)	0.83 (+0.34)*
Cholesterol mmol/L	4.25 (+1.14)	3.96 (+0.96)*
LDLC mmol/L	2.62 (+1.06)	2.52 (+0.84)
HDLC mmol/L	1.15 (+0.21)	1.62 (+2.30)

*Statistically significant ($P<0.05$)
Conclusion
The use of liraglutide in childhood obesity has shown improvements in BMI and metabolic profile. This shows the potential it has on reducing long-term complications and co-morbidities, such as cardiovascular and liver disease.

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Developing TechnOlogy to Support ChAnge (TOSCA tudy) for young people and their families seen in the complications of excess weight service

Brioney Gee[1,2], Bonnie Teague[1,2], Matt Farrar[3], Victoria Farrar[3], Dorothy Szinay[1], Ken Ong[4], Li Chan[5,6], Ben Jackson[7], Felix Naughton[8], Jon Wilson[1,2] & Emma Webb[1,9]
[1]Norwich Medical School, University of East Anglia, Norwich, UK; [2]NSFT Research, Norfolk and Suffolk NHS Foundation Trust, Nowrich, UK; [3]Nudg, 71-75 Shelton Street, Covent Garden, London, UK; [4]University of Cambridge, Cambridge, UK; [5]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University, London, UK; [6]Department of Paediatric Endocrinology, The Children's Hospital at the Royal London Hospital, Whitechapel, London, UK; [7]Eastern Academic Health Science Network, Cambridge, UK; [8]School of Health Sciences, Norwich, UK; [9]Jenny Lind Children's Hospital, Norfolk and Norwich University Hospital NHS Foundation Trust Colney Lane, Norwich, UK

Background
Complications of excess weight (CEW) clinics were commissioned by NHSE in 2021 to be leaders in the field of paediatric obesity using innovative models to deliver the highest quality patient care. Technological approaches offer a widely accessible tool which could potentially complement current clinical models of care. This study aims to explore children and young peoples (CYP) views on whether digital technology could/should be used to enhance CEW clinic support.
Method
Research ethics permission was obtained and written informed consent taken. Clinical academics worked with health technology company LovedBy, and a PPI co-investigator, to run one focus group and two workshops with young people seen in the CEW clinic. These sessions focused on understanding the health priorities of CYP and their families, the barriers and facilitators to making behavioural changes, and their views on co-designing ways that technology could

be used to support young people to make changes to achieve their health goals.
Results
13 CYP (4 male), with a mean age of 13.8 years (range 10.2–15.8) participated. The focus group identified that mental health was a key priority for CYP when they considered what a healthy life means to them. Barriers to good health included; financial constraints, poor sleep and anxiety with helpful factors including; positive stories and guidance on social media, communicating with others and family. Workshop one mapped out a day in the life of CYP. CYP reporting feeling tired, anxious, hungry, annoyed and angry at the start of the day with worries around sleep being a common theme in the evening. Workshop two demonstrated that young people would value technology which delivers information in the form of social stories delivered by their peers. It also highlighted the need for a face-to-face support group alongside any technology developed.
Conclusion
There is a desire from CYP seen in the CEW service for content developed for young people, created by young people. We hope to develop and assess the impact of these resources in a future study. Alongside any technological offering we will develop a peer support network with some face-to-face elements to complement virtual resources.

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A contextual evaluation of complications of excess weight (CEW) clinics in the Midlands region, England

Simon Harvey[1], Pankhuri Sahare[1], Louise Melbourne[2], David Elliott[3], Renuka Dias[4] & Pooja Sachdev[5]
[1]NHS England, Nottingham, UK; [2]NHS England, Birmingham, UK; [3]Office for Health Improvement and Disparities, Birmingham, UK; [4]Birmingham Women and Children's Hospital, Birmingham, UK; [5]University Hospital Nottingham, Nottingham, UK

Child obesity is a major public health concern in England and worldwide. It is a risk factor for the onset of type 2 diabetes and other comorbidities. Young people from the most deprived communities, from ethnic minority backgrounds or with learning disabilities are particularly at risk. NHS England funded the establishment of Complications of Excess Weight (CEW) pilot clinics, two of which serve the Midlands region. These provide specialist multidisciplinary whole-family support to young people living with severe obesity and a comorbidity related to their weight. A realist theory-informed qualitative evaluation, led by NHSE Midlands and OHID Midlands was conducted to understand how the clinics aligned with local obesity care services and population need. Four group interviews were conducted on Microsoft Teams between November 2022 and April 2023; they included CEW clinical leads, local public health and healthcare commissioners and commissioned weight management service providers from the Midlands. The discussions were supported with epidemiological data and evidence from literature reviews. The conversations were transcribed and thematically analysed. Initially, CEW was framed as a hospital-based, clinically led service, which was accessible via secondary care referral. While offering a bespoke and personalised approach, eligibility and outcomes were framed in strongly clinical terms (BMI centile threshold and comorbidities, weight and comorbidity management). However, it emerged that the success of the clinics also depended on alignment and partnership with local obesity care and social support services. The young people and their families who accessed the service had highly complex social and health needs, including a high proportion with learning disability and autism spectrum disorders and were not well served by existing services. To improve engagement and achieve positive clinical outcomes, CEW clinics needed to address the wider social needs of the family and reduce socio-economic barriers to access. A sustainable outcome included improved social outcomes for the family as well as clinical improvements. The evaluation highlighted opportunities to improve integration of CEW with local services in the Midlands and to deliver specialist support in a way that is sensitive to local need and in a way that reduces inequalities in access, experience and outcomes.

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P66

A higher proportion of physical and mental health CEW in areas of higher socio-economic deprivation demands urgent action: Comparative data across two regions of UK

Louise Apperley[1], Katherine Hawton[2,3], Jennifer Parkinson[1], Meghan Owens[4], Claire Semple[2], Amy Fitzgerald[2], Shelley Easter[2], Kate Clark[1], Kim Lund[1], Ellie Clarke[1], Dinesh Giri[2,3], Julian Hamilton-Shield[4,2] & Senthil Senniappan[1]
[1]Alder Hey Children's Hospital, Liverpool, UK; [2]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundations Trust, Bristol, UK; [3]University of Bristol, Bristol, UK; [4]NIHR Biomedical Research Centre (Nutrition Theme), University of Bristol, Bristol, UK

Introduction
NCMP (National Childhood Measurement Programme) data has highlighted a higher prevalence of childhood obesity in highly deprived areas, however the prevalence of complications from excess weight (CEW) in relation to social deprivation has not been previously reported. The aim of this study is to compare the demographic data along with CEW in children and young people (CYP) with obesity being managed at two different centres in the UK, with a very different socio-economic background.
Methods
Retrospective clinical data (101 patients at site 1 and 84 at site 2) was collected of all new patients seen over a 12-month period (March 2022–February 2023) in two tier-3 multidisciplinary weight management services across the UK (Liverpool and Bristol). Deprivation was compared using IMD (index of multiple deprivation) deciles.
Results
The results are detailed in Table 1. The mean age was 14.1 years (3–17) and 11.8 years (3–17) respectively at sites 1 and 2. Site 1, the most deprived area, observed a higher BMI (body mass index), percentage body fat and a higher rate of CEW. The levels of mental health complications including depression and anxiety were also higher in the most deprived area.
Conclusion
We have shown, for the first time, that a higher level of socio-economic deprivation is associated with a higher proportion of physical and mental health CEW in CYP. The data highlights the challenges in managing obesity-related complications in areas with high socio-economic deprivation. A targeted whole systems approach is required to reduce long term morbidity and mortality associated with severe obesity with a special focus on areas with higher indices of socio-economic deprivation.
Table 1

	Site 1	Site 2
IMD decile 1 (most deprived) %	58.2	21.7
IMD decile 10 (least deprived) %	2.0	7.2
White British	81.4	64.9
Mean weight (s.d.) kg	105.2 (+31.0)	79.9 (+33.1)
Mean BMI (SDS) kg/m2	39.4 (+3.7)	33.2 (+3.4)
% Body fat (s.d.)	51.1 (+8.2)	45.9 (+7.9)
Non-alcoholic fatty liver disease %	19.8	15.5
Dyslipidaemia %	51.9	51.0
Idiopathic intracranial hypertension %	7.9	1.2
Impaired glucose tolerance %	10.2	1.2
Depression %	13.1	1.2
Anxiety %	35.4	15.5

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Making every contact count – reconnecting oral health to holistic paediatric care in the management of childhood obesity

Jessica Large[1], Nivedita Aswani[2], Natalie Selby[2], Zoe Marshman[3], Joanne Charlesworth[4], Thomas Dyer[3], Emma Bingham[5] & Adrian Jowett[5]
[1]Paediatric Dentistry Department, Charles Clifford Dental Hospital, Sheffield, UK; [2]Sheffield Children's Hospital, Sheffield, UK; [3]Dental Public Health. University of Sheffield, Sheffield, UK; [4]Oral Health Promotion Manager Community and Special Care Dentistry, Sheffield, UK; [5]University of Sheffield. School of Clinical Dentistry, Sheffield, UK

Objectives
Sugar consumption is a common risk factor for dental disease, obesity and type 2 diabetes. Complications from Excess Weight clinics (CEW) provide children and young people (CYP) living with obesity and associated co-morbidities with a holistic plan to achieve healthier lifestyle practices. Children living with excess weight are more likely to experience dental decay. A collaboration between CEW clinics and local dental services aims to improve oral health (OH) and dietary habits of CYP. Student dental professionals' inclusion in clinics aims to better equip dental teams to manage affected CYP in the future.

Methods
CEW teams have observed a high proportion of CYP are at high risk of dental decay, erosion and periodontitis. Many do not access a dentist and are from socioeconomically disadvantaged backgrounds. A pathway has been developed to facilitate access to dental care, including via flexible commissioning, for urgent/routine care. Also, a dental hygiene and therapy student outreach programme is underway. The aim is for regular student presence in CEW clinics to create a 'one-stop' appointment where CYP can access OH advice and preventative treatment, as well as access further care as required. Student reflective reports and CYP feedback will help inform future service development.
Results
Students provide OH advice having insight into food and drink preferences, eating patterns, sleep disruption and the influence of social determinants and co-morbidities on oral and general health. CYP attending CEW clinics are questioned on their OH practices. Family support workers now receive OH training to encourage good practice as part of their home assessments. Advice on preventing decay and erosion and support in finding an NHS dentist are now incorporated into the Service's App ('My Health-Boost').
Conclusion
This service development champions inter-professional collaboration aligning with the Making Every Contact Count approach and CORE20PLUS5. It has potential to improve access to dental care for a high decay-risk cohort of CYP and support them with their weight and OH.

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Case report: Potocki-lupski syndrome (PTLS) with obesity

Eiman Naghmuish[1], Marisa Clemente[2] & Kamal Weerasinghe[2]
[1]Betsi Cadwaladr University Health Board, Wrexham, UK; [2]Betsi Cadwaladr University Health Board, Wrexham, UK

Case report
Potocki-Lupski Syndrome (PTLS) with obesity
Eiman Naghmuish[1], Marisa Clemente[1], Kamal Weerasinghe[1]
[1]Department of Paediatrics, Wrexham Maelor Hospital, Betsi Cadwaladr University Health Board, The UK.
Introduction
Potocki-Lupski syndrome (PTLS) is a rare genetic disorder affecting 1:20.000 people worldwide, it is caused by a duplication of a specific region on chromosome 17q12. PTLS is typically considered a de novo (sporadic) condition. However, in some cases the duplication can be inherited as an autosomal dominant manner, and parent to child transmission has been reported.
Case report
A 5 year old girl who has been referred to the endocrine clinic in view of: Signs of early puberty Obesity with a weight 25kg above the 99.6th centile, height 2 cm above the 99.6th centile, and BMI 33.8 >99.6th centile 3-Mood changes She was born at term and her birth weight was 3.300 kg (25th–50thcentile), and parents started to be concerned about her weight when she was 3 years old. She had numerous investigations for signs of early puberty, her bone age at 3 years and 11 months was 6 years, pelvic ultrasound scan has confirmed her uterus remains tubular, normal MRI head, short synacthen test showed a normal response, while her LH RH stimulation test has not seen significant LH rise and the results are in keeping with pre-pubertal stage. Her genetics tests recently revealed the diagnosis of 17q12 microduplication syndrome, a normal obesity gene panel.
Discussion
PTLS is a developmental disorder characterized by cognitive, behavioral, and medical manifestations. Cognitively, most individuals present with developmental and intellectual delay, speech and language delay. Behaviourally, issues such as attention-deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), or autism spectrum disorder (ASD). Medically, it is characterized by hypotonia, congenital heart disease, oropharyngeal dysphagia leading to faltering growth, hypoglycaemia associated with growth hormone deficiency, and mild facial dysmorphism. Recent studies have suggested a potential association between 17q12 microduplication syndrome and an increased risk of obesity, however, the underlying mechanisms are not fully understood. Every individual with PTLS is unique, and the manifestation and severity of symptoms can vary.

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Pituitary and Growth 1

P69

Segmental growth relationships between fetal and postnatal measures in the Manchester BabyGRO Study

Kathryn McCabe[1,2], Andrew Whatmore[1], Lucy Higgins[1,2], Adam Stevens[1], Ed Johnstone[1,2], Peter Clayton[1,2] & Reena Perchard[1,2]
[1]The University of Manchester, Manchester, UK. [2]Manchester University NHS Foundation Trust, Manchester, UK

Background
Using small for gestational age (SGA) as a surrogate for fetal growth restriction, previous studies link adverse intrauterine environments to greater cardiometabolic risk. However, a fetus may undergo suboptimal fetal growth (SFG) without being SGA. The Manchester BabyGRO Study focused on recruiting pregnancies at greater risk of SFG, including pregnancies with low PAPP-A, where a pattern of reduced skeletal growth has been described(1). Associations were explored between fetal weight centile and postnatal indicators of accelerated/ catch-up growth, other potential fetal indicators of postnatal adiposity trajectory were not explored.
Aim
Investigate relationships between segmental growth trajectories and central adiposity in fetal and postnatal life.
Methods
Components of the Hadlock formula used to calculate estimated fetal weight (EFW) in the Manchester BabyGRO Study were: head circumference (HC), abdominal circumference (AC), and femur length (FL). AC was selected as a marker of central adiposity; FL as a marker of skeletal growth. Δfetal_AC ([birth AC minus 23 week AC]/days), 23 week fetal FL, and postnatally Δ0-3_AC ([three-month AC minus birth AC]/days), Δ0-6_AC, Δ0-12_AC, Δ0-3_leg ([three-month leg length minus birth leg length]/days), Δ0-6_leg and Δ0-12_leg were calculated. Parametric data were assessed using Pearson's correlation, Spearman's correlations assessed non-parametric data to determine significant correlations between fetal and postnatal trajectories, P value <0.05 was considered significant.
Results
78/80 participants had estimated fetal biometry <200 days' gestation (39/78 male offspring), 59%/15%/12% White/ Asian/ Black and 14% other ethnicity, Δfetal_AC correlated negatively with Δ0-3_AC ($r=-0.453$, $P<0.001$) and Δ0-6_AC ($r=-0.540$, $P<0.001$), but not with Δ0-12_AC ($r=-0.16$, $P=0.330$). No correlations were observed between ultrasound femur length and postnatal leg length trajectories.
Conclusion
Relationships between fetal and postnatal AC trajectories suggest Δfetal_AC may represent a fetal marker of undesirable postnatal adiposity trajectory. Associations between pre- and postnatal skeletal measures were not detected. Postnatal femur length measurements would allow for direct comparisons and add value to future studies.
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Novel insights into genetic causes of childhood growth failure from patients recruited to the 100 000 Genomes Project

Miho Ishida, Letizia Vestito, Avinaash Maharaj, Valentina Cipriani, Damian Smedley & Helen Storr
William Harvey Research Institute, Queen Mary University of London, London, UK

Short stature (SS), defined as height ≤ -2 SDS for a given population, comprises ~50% of new patient referrals to paediatric endocrine clinics. Since >80% SS children in the UK do not receive a clear diagnosis, enhanced genetic testing and stratification is a fundamental need. Whole-genome sequencing (WGS) was offered to rare disease patients recruited to the 100 000 Genomes Project (100KGP), leading to new clinical diagnoses in ~25% of participants. The 100KGP analysis pipeline uses disease-specific virtual gene panels, with focus on coding regions and canonical splice sites. Genes outside the panel, intronic variants impacting non-canonical splice sites and copy number variations (CNVs) remain uninvestigated. Our study aimed to identify molecular causes of SS in unsolved individuals recruited to the 100KGP. From 72 947 participants recruited to the rare disease cohort, 1996 SS probands were identified, of which 1602(80%) remained unsolved. WGS data from unsolved cases were interrogated to investigate coding/intronic variants affecting non-canonical splice sites in our

wider gene panel, CNV and uniparental disomy (UPD). Burden analysis was used to investigate the effects of rare damaging coding variants on SS. In unsolved probands, 509 previously unreported coding (83 splice site, 41 frameshift, 35 stop gain, 350 missense) and 217 intronic predicted highly pathogenic variants were identified, respectively. This included a novel deep intronic variant in HMGA2 predicted to create a cryptic donor site and possible pseudoexon inclusion in a Silver–Russell Syndrome patient. CNV analysis identified variants predicted pathogenic at both previously established (1q21, 22q11.2) and novel regions. Burden analysis revealed statistically significant associations with genes implicated in growth. 100KGP has made a significant contribution to the healthcare community through its unprecedented scale of testing and depth of information it has generated. This study shows that WGS has clear advantages in its ability to simultaneously detect coding and deep intronic SNV, CNV and UPD, and its potential to improve diagnostic rate. This work is particularly relevant to those investigating endocrine diseases with heterogenous molecular origin. Application of WGS in a clinical setting could improve diagnosis/clinical care for patients/families and discovery of new candidate genes for targeted clinical treatments.

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P71

The oxytocin system in craniopharyngioma: A systematic review

Amy Mann[1], Jennifer Kalitsi[1,2], Khushali Jani[3], Daniel Martins[1], Ritika R Kapoor[3,4] & Yannis Paloyelis[1]
[1]King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK; [2]King's College London, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, Child and Family Health Nursing, London, UK; [3]King's College London, Faculty of Medicine and Life Science, London, UK; [4]Department of Paediatric Endocrinology, Variety Children's Hospital, King's College Hospital NHS Foundation Trust, London, UK

Background
Craniopharyngioma is a benign tumour involving the hypothalamic and pituitary regions that are involved in the production and secretion of oxytocin. Research has shown that dysfunction of the oxytocin system is associated with neurobehavioural and metabolic outcomes, but less is known for its role in patients with craniopharyngioma, largely due to varied study designs and heterogenous methods of assessing the oxytocin system. This systematic review aimed to assess the extent to which the oxytocin system is involved in craniopharyngioma and its association with neurobehavioural and metabolic abnormalities.
Methods
This review was pre-registered on PROSPERO (CRD42023397966). PubMed, EMBASE, PsycInfo, and Cochrane Central Register of Controlled trials were searched from inception to January 19 2023 using key terms *craniopharyngioma* and *oxytocin*. Reference lists of included studies and relevant reviews were searched. All observational studies assessing the oxytocin system and neurobehavioural or metabolic (e.g., body mass index) abnormalities in humans with craniopharyngioma were independently reviewed by two authors.
Results
Of 61 articles screened, eight studies were included. One case report found improvements in food preoccupation and BMI z-score which decreased from 1.77 SDS (96th percentile) to 0.82 SDS (79th percentile) following 6 IU/day of intranasal oxytocin over 48 weeks. Another case report found no improvements in food-related obsessive–compulsive behaviours, but did find improvements in social behaviours (dosage 4 IU/day; ~60 weeks). Of studies assessing the endogenous oxytocin system, no significant differences in baseline fasting or post-prandial serum oxytocin concentrations were reported between craniopharyngioma patients and controls. However, craniopharyngioma patients were found to have blunted-oxytocin release following exercise stimulation and this was associated with greater autistic traits, reduced hedonia for social interactions, and higher state anxiety. One study reported improved emotion identification following single-dose (24 IU) intranasal oxytocin in patients with anterior hypothalamic damage compared to those with anterior and posterior damage.
Conclusions
Definitive conclusions regarding the oxytocin system in craniopharyngioma remain to be established due to the limited studies and lack of homogenous methods used in this population. Nevertheless, this review found that the oxytocin system may be compromised in craniopharyngioma and present a plausible mechanism underlying neurobehavioural and metabolic problems in this population.

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P72

Using basal LH to predict response on luteinising hormone releasing hormone stimulation test

Katie Francis[1], Toby Candler[1] & Corey Pritchard[2]
[1]Department of Paediatric Endocrinology, Bristol Royal Hospital for Children, Bristol, UK; [2]Department of Biochemistry, University Hospitals Bristol and Weston, Bristol, UK

Introduction
Luteinising Hormone Releasing Hormone stimulation test (LHRH) is the gold standard test for diagnosing central precocious puberty (CPP). However, previous studies have advocated using a single LH (Luteinising Hormone) measure to diagnose CPP thus reducing the patient's investigative burden.
Method and aims
We assessed if i) baseline LH levels predicts response on LHRH test ii) the timing of basal LH measurement influences its predictive value. A retrospective review of children undergoing LHRH testing at Bristol Royal Hospital for Children between February 2019 to January 2023 was conducted. LH was measured using Roche Sandwich Immunoassay, 3rd generation (<0.1 IU/L lower limit of detection).
Results
111 tests were conducted ($n=99$ in females, $n=12$ in males). LH and FSH levels were measured at 30 min and 60 min after LHRH administration. Those with a peak LH ≥5 and LH predominance were categorised as positive, peak LH ≥5 but FSH (follicle stimulating hormone) predominance as borderline, and peak LH <5 was categorised as negative. Of the 28 positive tests, only 2 had baseline LH <0.3 and both were afternoon tests. Of the 70 negative tests, 2 had baseline tests LH ≥1, both morning tests. The table below summarises the predictive values for different basal LH levels.

Baseline	Sensitivity	Specificity
LH ≥ 0.1	92.9%	77.1%
LH ≥ 0.3	92.9%	88.0%
LH ≥ 0.3 (morning measurement)	100%	85.7%
LH ≥ 0.3 PM (afternoon measurement)	91.3%	88.7%
LH ≥ 0.5	85.7%	92.8%
LH ≥ 1	53.6%	96.4%
LH ≥ 2	46.4%	98.8%

The mean tanner breast staging was higher in positive tests; 2.86 vs 2.10 ($P=<0.001$). There was no significant difference in testicular volume between positive and negative tests; 3.75 mL vs 4 mL ($P=0.72$).
Conclusion
Using a LH cut off of ≥ 0.3 provided the best balance of sensitivity and specificity and could be used to predict a positive LHRH test in the majority of cases. False negatives were more common if using afternoon basal LH samples and false positives more common if using morning basal LH samples to predict LHRH response. LH levels should be correlated with pubertal stage as part of the clinical assessment.

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P73

Significance of targeted gene panel sequencing in early childhood growth failure

Shaju Edavana, Uma Kumbattae & Emma Hawkes
Royal Stoke University Hospital, Stoke-On-Trent, UK

Early childhood growth failures are associated with significant diagnostic and therapeutic implications. Testing for a panel of genes associated with a poor growth has identified a diagnosis of 3M syndrome. Index case was born at 36 weeks' gestation with a birth weight of 1.88 kg (>2nd centile) and length 40 cm (<0.4 the centile) with head circumference 45 cm on 50th centile. Her initial assessment noted severe intrauterine growth retardation pattern. She had normal Skeletal survey and Achondroplasia gene test and Russel Silver test was negative Both parents are healthy, mid parental height on 25 the centile and were first cousins. Mother had previous 3 miscarriages and has 8-year brother with normal height. There is strong family history of short family members on both side of the family. She has Congenital hypothyroidism with normal thyroid scan and most likely transient hypothyroidism. She maintained her weight on 0.4th centile (−3SDS) and height far below 0.4th centile (−4SDS). She has seen Dietitians who feels that she has appropriate calory intake. She has started walking at 14 months of age. She continues her follow up under Endocrinology and was seen by Clinical Geneticist and Orthopedics. Recently we commenced her on growth hormone therapy as per SGA license at 2 ½ years of age and under review on the response to growth hormone treatment. She was found to have an alteration in

both copies of her CCDC8 gene. This is associated with a diagnosis of 3 M syndrome type 3. 3 M syndrome has many similarities with Russell–Silver syndrome with growth difficulties and normal head circumference. In addition to short stature, other features that can be seen in individuals with 3 M syndrome include prominent heels, hip dysplasia and in some individuals' short neck or short chest. This diagnosis is not usually associated with developmental delay or learning difficulties. Integration of genetic sequencing in cases of early childhood growth failure is warranted to aid diagnosis. Early diagnosis is essential so that appropriate support and genetic counselling can be given.

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P74

Effect of steroid therapy in a 16-year-old girl with lymphocytic hypophysitis – case report

Elżbieta Moszczyńska[1], Marta Baszyńska-Wilk[1], Patrycja Dasiewicz[1], Aleksandra Tutka[1], Anna Smorczewska Kiljan[3], Magdalena Marszał[2] & Iwona Pakuła-Kościesza[3]
[1]Department of Endocrinology and Diabetology, The Children's Memorial Health Institute, Warsaw, Poland; [2]Department of Pediatrics, Nutrition and Metabolic Diseases, The Children's Memorial Health Institute, Warsaw, Poland; [3]Department of Radiology, MR Unit, The Children's Memorial Health Institute, Warsaw, Poland

Introduction
Lymphocytic hypophysitis is rare in children, with only <100 cases described in the medical literature, of which only a few are biopsy-proven. Usually results in hypophysis and pituitary enlargement. Arginine vasopressin deficiency and growth retardation are the most significant presenting symptoms in children with hypophysitis, different from teenagers in whom adrenal insufficiency, hypogonadism, headache, or diplopia might be the leading manifestations. Treatment consists of steroids or immunosuppressive therapy.
Case presentation
A 16-year-old previously healthy girl presented with headaches, vomiting, lethargy, binocular strabismus, and 2 months history of polydipsia and polyuria. The endocrine evaluation was based on thyroid and adrenal function assessment, insulin-like growth factor 1 (IGF-1) serum level measurement, gonadotropins, estradiol, and prolactin. The concentration of immunoglobulins, antithyroglobulin antibodies (anti-Tg), thyroid peroxidase antibodies (anti-TPO), tumor markers such as alpha-fetoprotein (αFP), and beta-human chorionic gonadotropin (βhCG), QuantiFERON test, angiotensin-converting enzyme (ACE) were determined. X-ray chest, abdomen computed tomography (CT), and brain magnetic resonance imaging (MRI) were performed. Endocrine investigations showed central hypothyreosis [thyroid-stimulating hormone (TSH) 0.6100 mIU/l (*N*:0.48–4.17), free thyroxine (fT4) 0.67 ng/dL (*N*:0.83–1.43)] and arginine vasopressin deficiency. Dehydroepiandrosterone sulfate (DHEA-S) was below the normal range: 30.8 (98.3–413.4) [μg/dL]. Estradiol concentration was 16.49 pg/mL (*N*:21.9 – 297.2). Normal follicle-stimulating hormone (FSH) level, luteinizing hormone (LH), and prolactin were noticed. The brain MRI identified a T2-hyperintense sellar/suprasellar lesion $10\times 9\times 21$ mm with a thick rim of enhancement and minimal sella expansion, with pituitary stalk thickening to 4.5 mm. The ophthalmological assessment showed normal visual acuity and fields. Treatment was started with dexamethasone administered intravenously (followed by prednisone per os), desmopressin, and levothyroxine. Headaches, strabismus, and lethargy were completely resolved. After 2 months of steroid treatment, a brain MRI did not reveal the previously described pituitary focal lesion but only a heterogeneous image of the pituitary gland and stalk, indicating an inflammatory process.
Conclusion
Lymphocytic hypophysitis is a rare cause of multihormonal hypopituitarism in children. Differential diagnosis includes neoplasms and other inflammatory diseases. Steroid therapy was effective in our patient. Careful follow-up is necessary to manage endocrine deficiencies, and there is the possibility of recurrence of pituitary inflammatory changes.

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P75

Growth hormone deficiency associated with *BRAF*-related cardiofaciocutaneous syndrome

Amy Mann[1], Simon Chapman[2], Naz Raoof[3], Leema Robert[4] & Ritika R Kapoor[2,5]
[1]King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK; [2]Department of Paediatric Endocrinology, Variety Children's Hospital, King's College Hospital NHS Foundation Trust, London, UK; [3]Department of Paediatrics, Strabismus and Neuro-ophthalmology, Moorfields Eye Hospital, London, UK; [4]Clinical Genetics Department, Guy's and St Thomas' Hospital, London, UK; [5]King's College London, Faculty of Medicine and Life Science, London, UK

Background
Cardiofaciocutaneous (CFC) syndrome is a rare disorder characterised by multiple abnormalities including congenital heart disease, craniofacial dysmorphology, ectodermal abnormalities, developmental delay, and epilepsy. Case reports of growth hormone (GH) deficiency, hyperprolactinemia, and precious puberty have been reported in association with CFC syndrome. A recent case series and gene knockout study highlighted the mechanistic role of CFC syndrome-causing gene, B-Raf proto-oncogene (*BRAF*), in pituitary gland development and subsequent hypopituitarism. Here, we present a case showing the involvement of *BRAF* in hypopituitarism associated with CFC syndrome.
Case presentation
Our patient was diagnosed with CFC syndrome caused by a heterozygous missense variant (c.770A$>$G) in exon 6 (p.Q257R mutation) of the *BRAF* gene. His phenotype includes distinctive facial features, left ventricular hypertrophy, developmental delay, hypotonia, feeding problems, undescended testis, and epilepsy. Ophthalmological investigations identified bilateral optic atrophy. He was referred to endocrinology for short stature at 4.6 years of age (ht SDS -4.00). GH deficiency was diagnosed following an inadequate GH peak of 4.76 mU/L during a glucagon stimulation test and undetectable serum IGF-1. ACTH and TSH deficiency were excluded. Additionally, he experiences symptoms characteristic of hypothalamic syndrome including sleep disturbance and social-communication difficulties. Treatment with 0.025 mg/kg per day of GH led to marked improvements in gross motor skills and mobility. His height centile and serum IGF-1 concentrations however only improved after gradually increasing the dose to 0.05 mg/kg per day. His current height at 12.3 years lies on the 5th centile (MPH between the 9th and 25th centile). Serum IGF-1 concentrations have remained in lower quartile (23.4 nmol/l; 6.4–68.1) despite relatively high GH doses, suggesting possible GH insensitivity. Magnetic resonance imaging identified hydrocephalus which was treated with a ventriculoperitoneal shunt, but showed otherwise normal brain and pituitary gland.
Conclusion
We describe the second report of *BRAF* mutation in association with GH deficiency in a patient with CFC syndrome. The response to GH therapy is similar to the previous report, suggesting possible co-existent GH insensitivity. Along with GI and cardiac defects, GH deficiency must be considered as a cause of short stature in CFC syndrome.

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P76

Monozygotic twins with short stature due to temple syndrome and GH plus GnRHa treatment in one twin

Claudia Lattanzi[1,2], Louise Wilson[3] & Evelien Gevers[1]
[1]Barts Health NHS Trust, Royal London Children's Hospital, Department of Paediatric Endocrinology, London, UK; [2]University of Parma, Dept. of Medicine and Surgery, Unit of Paediatrics, Parma, Italy; [3]Great Ormond Street Hospital, Dept. of Genetics, London, UK

Temple syndrome is due to loss of methylation at 14q32. Features are prematurity, low birth weight, hypotonia, feeding difficulties, short stature and early puberty, as well as small hands and feet, mild learning disability and variable obesity. We report monozygotic twins with Temple syndrome. Twin1 was born at $31+2$ weeks with mild SGA (1120g, $<10^{th}$ centile), head circumference 27 cm, undescended testes, severe hypotonia and laryngomalacia. He developed camptodacyly, mild learning difficulties and scoliosis requiring rodding. He started Levothyroxine for mild hypothyroidism aged 2 months. Glucagon testing showed a GH peak of 7.6 ng/mL with normal IGF1. IGF1 continued to be in the lower third of the normal range with a low normal IGFBP3. He received GH for SGA from age 9.5yrs when his height was -2.7S.D.. He responded well, but developed CPP with quickly progressing puberty. Bone age was 12.0yrs at a chronological age of 10.8 yrs. GnRHa was started with delay due to the pandemic, aged 11.2yrs when height was -0.86S.D. and testes volumes 12/12 mL. At 12.8yrs his height was 144.8 cm (-1.13S.D.), height velocity (HV) 3.1 cm/yr, BMI 22.3 kg/m^2 ($+1.60$ S.D.), G3P3A2 testes 8/8–10 mL and advanced bone age of 14.0 yrs. His twin brother was born without SGA and did not receive GH treatment. He had bilateral camptodactyly, mild scoliosis and absence of lateral incisors. His pubertal onset was before the age of 10, but he had reduced follow up due to COVID, and was well developed into puberty (P3G3A2 testes 8/10–12 mL) with a good growth spurt (9.7 cm/yr) at 11.2 yrs. GnRHa was not started. Bone age was 12.66 yrs at CA 10.8yrs. At 12.8 yrs, his height is

145.8 cm (−1.0 s.d.), height velocity 1.9 cm/yr, BMI 22.1(+1.5s.d.), G3P3A2, testes 12–15 mL with an advanced bone age of 16.3 yrs. 100K genome study revealed no abnormalities. 14q methylation testing was performed subsequently which revealed Temple Syndrome. In conclusion, Temple syndrome needs to be considered in patients with short stature and additional features or an SRS like phenotype. A combination of GH and GnRHa may improve final height.

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Thyroid 1

P77

The dynamic response of the thyroid hormone axis in central hypothyroidism

Valentina Zaccarini[1], Susan Vickery[2] & Tony Hulse[3]
[1]Maidstone & Tunbridge Wells NHS Trust, Tunbridge Wells, UK; [2]Maidstone & Tunbridge Wells NHS Trust, Maidstone, UK; [3]Evelina London Children's Hospital, London, UK

Introduction
The diagnosis of central hypothyroidism can be challenging and confused with other causes of low thyroxine concentrations without TSH elevation. The response of the thyroid hormone axis before and after treatment is reported in children with Central Hypothyroidism [CH] as part of an exercise aimed at validating free thyroxine reference ranges.
Methods
Roche Elecsys Cobas TSH and FT4 immunoassays were used. TSH and free T4 (FT4) concentrations were reported in children ($n=18$) with confirmed CH before and after treatment. Confirmation of the diagnosis was made by finding MRI abnormalities [4 children] or the presence of other pituitary hormone abnormalities [15 children]. The age range of patients was from <1 month to 17 years. Mean (±s.d.) values are quoted for normally distributed data; otherwise median (range) values are quoted, with median groups compared using the Kruskall Wallis test.
Results
At diagnosis the mean FT4 concentration was 8.4 (± 2.0) pmol/L. Two children were above the lower FT4 cut-off of 10.8 pmol/L. Mean TSH concentration was 3.2 (± 2.2) mU/L where only 1 child had an undetectable TSH, 15 children were within their age-related reference range and 2 children were above. There was no correlation between FT4 and TSH concentrations prior to treatment. After treatment the median FT4 concentration was 16.0 (12.7 to 18.7) pmol/L. TSH concentration was suppressed from the pre-treatment concentration in 6 children and was below the reference range in 4. The post treatment TSH clearly fell into two groups ($P<0.001$): those with a normal TSH concentration and those in whom the TSH was suppressed.
Conclusions
In Central Hypothyroidism at diagnosis, free thyroxine concentrations may overlap with the lower part of the reference range and the TSH may be low, normal or slightly raised. It is rarely undetectable. After treatment the TSH suppresses indicating that the feedback control loop is still active in CH. However, CH patients clearly separate into two groups: those with detectable and those with undetectable TSH concentrations on treatment. This may reflect the differing pathological causes of the CH and may indicate a new way of classifying Central Hypothyroidism.

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P78

Outcome of a case of foetal goitre

Sachin Unny & Uma Kumbattae
Royal Stoke University Hospital, Stoke-On-Trent, UK

28-year-old pregnant female had been followed with serial scan and thyroid function tests with concern of foetal goitre. She had a previous stillbirth at term where a goitre was found at post-mortem and cause of death was hypothesized to be high output cardiac failure secondary to thyrotoxicosis. Mother's thyroid function and thyroid antibodies were negative throughout pregnancy. Baby girl was born at 33 weeks by Caesarean Section with a birth weight of 1.785 kg She had a small goitre and needed CPAP for 24 hrs. Her initial thyroid function test on day 2 of life showed TSH >150 mU/L and T4 8 pmol/l. She was started on Levothyroxine 25 µg daily which had to be reduced gradually to 12.5 mg alternate days by day 21 due to persistent high T4. Her Anti-TPO antibodies and TSH receptor antibodies were negative, Neck USS showed slightly bulky thyroid gland and Technetium scan showed normal uptake. Her ECG showed sinus rhythm with brief junctional rhythm with normal echocardiogram. Baby failed the new-born hearing test. On follow up, normal growth and development. No goitre with a normal ECG and Echo. Levothyroxine was stopped at 15 months of age. She was found to have moderate bilateral sensory neural hearing loss and required hearing aids from 5 months of age. One of the siblings was also wearing hearing aids. This initiated molecular genetics test for Pendred Syndrome which was confirmed. Genetic tests on parents were awaiting. Pendred Syndrome is an autosomal recessive genetic condition caused by mutations, in a gene called SLC26A4 on chromosome 7. Pendred Syndrome accounts for 10% hereditary hearing loss and causes early or progressive hearing loss in children, significant enough to have a Cochlear implant. Thyroid gland enlargement can develop in adolescence or later part of life, but thyroid functions are usually normal. People with this syndrome may have their balance affected due to the involvement of the vestibular system. This case shows the relevance of a focused family history, in order to initiate appropriate investigation for long-term management.

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P79

Cardiac presentation of a common endocrine condition

Sachin Unny, Agampodi Gunasekara, Uma Kumbattae & Pavanasam Ramesh
Royal Stoke Univeristy Hospital, Stoke-On-Trent, UK

Case summary
7 yr old girl referred by GP to the cardiology clinic with heart murmur. Mother reported to GP about facial and periorbital puffiness intermittently for the last 2 years. Cardiology clinic review showed 1/6 short systolic murmur with small pericardial effusion. Pericardial effusion was initially thought to be possible post viral illness and the facial puffiness which remained unexplainable. A repeat Echo at 3 months later showed persistence of pericardial effusion, hence blood test including thyroid function was done as hypothyroidism is one of the rare causes of pericardial effusion and showed a high TSH >150 mU/L free T4 <1 pmol/L. On further review in the endocrine clinic mother reported slow growth and she was very cold all the time, with swollen feet. On physical examination she had dry skin, coarse facies, facial puffiness, swelling of hands and feet and no goitre Her weight was 30.8 kg >50 th centile height 124.6 cm, (2nd – 9th centile) with mid parental centile above 50 th centile. Insulin like growth factor was low (7 nmol/L), anti-thyroid peroxidase antibody was high (>3000 iu/mL), anti-tTG and anti-endomysial Ab were mildly elevated. Her bone age was delayed by 3 years. She was started on Levothyroxine and dose increase gradually. Her growth parameters improved significantly with height above 50th centile within 8 months of treatment, insulin growth factor normalised. She had lost 4 kg in weight in the first 3 months of starting treatment due to resolving pedal oedema then continue to improve in weight and maintained on 75th centile. Pericardial effusion resolved completely on repeat ECHO. She is under follow-up of gastroenterology for weakly positive coeliac screen but there is no family history of coeliac disease, and she has no gastrointestinal symptoms and awaiting duodenal biopsy for confirmation.
Discussion
Autoimmune hypothyroidism is the most common cause of acquired hypothyroidism children. Pericardial effusions are rare complication in children. Early recognition and replacement can prevent serious complications.
Conclusion
Growth assessment in children is essential across all paediatric specialities and helps to explore further relevant history to initiate appropriate investigations and management without delay.

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P80

Subclinical hypothyroidism in children, when to treat

Magdy Ahmed
Southend University Hospital, Southend, UK

Aim
The purpose of this review is to outline the key elements that should be taken into account when making a determination regarding the prescription of L-Thyroxine for a pediatric patient diagnosed with subclinical hypothyroidism (SH).
Methods
A systematic review of the literature was conducted to evaluate the current evidence regarding the management of subclinical hypothyroidism in children.

Results
For children who exhibit progressive thyroid deterioration due to underlying Hashimoto's thyroiditis, it is advisable to recommend therapy, especially if they present with goiters, hypothyroid symptoms, or have coexisting conditions such as Turner syndrome, Down's syndrome, or other autoimmune disorders. Furthermore, children with proatherogenic metabolic abnormalities may also benefit from treatment. Conversely, in cases of idiopathic or mild subclinical hypothyroidism (SH) without goiter, hypothyroid symptoms, or positive thyroid autoantibodies, treatment is not recommended. In the absence of intervention, regular monitoring of clinical status and thyroid function tests is necessary to identify children who may require treatment. Children with persistently mild elevations in thyroid-stimulating hormone (TSH) levels who are not receiving L-Thyroxine should undergo biochemical monitoring of thyroid function and reassessment of their clinical status every six months. The monitoring interval can be extended after two years of stable thyroid function tests
Conclusions
This review offers valuable insights into the management of subclinical hypothyroidism in pediatric patients, emphasizing the need for personalized treatment decisions based on clinical presentation, laboratory results, and underlying conditions. The study suggests that in children with chronic kidney disease (CKD), a TSH cutoff of 10 u/L may be appropriate for initiating thyroxine replacement therapy. Additionally, the review highlights the importance of recommending replacement treatment for children with subclinical hypothyroidism who have underlying Hashimoto's thyroiditis, progressive thyroid deterioration, goiters, hypothyroid symptoms, associated conditions like Turner syndrome or Down's syndrome or proatherogenic metabolic abnormalities. On the other hand, for children with idiopathic or mild subclinical hypothyroidism, treatment is not recommended, and regular monitoring of thyroid function and clinical status is advised to identify those who may eventually benefit from therapy. Further research is required to validate the optimal management approach for subclinical hypothyroidism in children.

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Adrenal 2

P81

National service evaluation of care for children and young people with congenital adrenal hyperplasia in the UK: Survey responses from patients and clinicians

Neil Lawrence[1,2], Irina Bacila[1], Xiaochen Ji[1], S Faisal Ahmed[3], Sabah Alvi[4], Louise Bath[5], Jo Blair[6], Tim Cheetham[7,8], Liz Crowne[9], Justin H Davies[10], Mehul Dattani[11], Evelien Gevers[12], Ruth Krone[13], Leena Patel[14], Ajay Thankamony[15,16], Tabitha Randell[17], Fiona Ryan[18], Sue Elford[19], Sallyann Blackett[19] & Nils Krone[1,2]
[1]The University of Sheffield, Sheffield, UK; [2]Sheffield Children's Hospital, Sheffield, UK; [3]The University of Glasgow, Glasgow, UK; [4]Leeds Children's Hospital, Leeds, UK; [5]Royal Hospital for Sick Children, Edinburgh, UK; [6]Alder Hey Children's Hospital, Liverpool, UK; [7]The University of Newcastle, Newcastle, UK; [8]Great North Children's Hospital, Newcastle, UK; [9]University Hospitals Bristol and Weston Foundation Trust, Bristol, UK; [10]University Hospital Southampton, Southampton, UK; [11]Great Ormond Street Hospital, London, UK; [12]London and Barts Health NHS Trust, London, UK; [13]Birmingham Women's and Children's Hospital, Birmingham, UK; [14]Royal Manchester Children's Hospital, Manchester, UK; [15]The University of Cambridge, Cambridge, UK; [16]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [17]Nottingham Children's Hospital, Nottingham, UK; [18]Oxford Children's Hospital, Oxford, UK; [19]CAH Support Group, Birmingham, UK

Aim
To quantify difference in service provision for children and young people (CYP) living with CAH across the UK.
Methods
A national service evaluation using online questionnaires circulated to patients and clinicians from secondary and tertiary UK centres managing CYP with CAH, and via the 'Living with CAH' support group mailing list.
Results
Total of 195 responses relating to patients aged 0–20 years (43 patients, 152 carers), as well as 34 clinicians from 33 hospitals. Only 11.8% of clinicians were 'completely satisfied' with the service provided, compared to 67.6% of carers and 76.2% of patients. Patients and carers reported confidence in managing the chronic aspects of CAH, but only 40.3% of carers felt confident in an emergency. Whilst 94.1% of clinicians reported providing formal training to families with CAH, over 80% of both patients and carers reported not attending what they considered formal training when compared to diabetes education courses, although comments reflected a wide variety of approaches to patient education in CAH. One third of clinicians report less than 1 hour of training, and 2/3 report training is done in less than 4 hours, with only 47.1% of clinicians always ensuring school is contacted directly. Appetite for further training was higher in carers (85.5%) than patients (54.8%), although further 'unsure' responses suggested formal training sessions would likely be well attended. There was good satisfaction among patients/carers regarding time dedicated to discussions about general wellbeing and management of CAH. However, carers reported psychological (48.0%) and cardiovascular effects (40.0%) were insufficiently addressed, clinicians also acknowledging these topics are rarely addressed alongside infertility and impact on adult height. Biochemical monitoring of treatment was broadly in keeping with international guidelines, with 66.7% of clinicians reporting regular use of dried blood spots, and 11.8% regular urinary steroid metabolites.
Conclusion
While there is overall good satisfaction with care provision among patients and carers with CAH in the UK, extra resources addressing the psychological impact of CAH and delivering formal training about the disease and its management would benefit patients and carers.

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P82

Cortisol measurement using immunoassay versus liquid chromatography–tandem mass spectrometry in infants with congenital adrenal hyperplasia

Elham Atiq[1], Laura Walker[2], Joanne Blair[1] & Senthil Senniappan[1]
[1]Department of Endocrinology, Alder Hey Children's Hospital, Liverpool, UK; [2]Department of Biochemistry, Alder Hey Children's Hospital, Liverpool, UK

Introduction
Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders that arise from enzyme deficiencies in biosynthetic pathways of the adrenal. The most common enzyme deficiency, 21-hydroxylase deficiency, results in cortisol deficiency, androgen excess and variable aldosterone deficiency. Current guidelines recommend a standard dose short Synacthen test (SDSST) is performed between 24 and 48 hours of life, with measurement of cortisol and androgens. Cortisol is measured routinely by chemiluminescent immunoassay (CLIA). However, there is cross-reactivity of cortisol with 17α-hydroxyprogesterone and 21-deoxycortisol in most CLIA assays, which are elevated in patients with 21-hydroxylase deficiency, giving a falsely higher cortisol level. Liquid chromatography–tandem mass spectrometry (LC–TMS) is highly specific and eliminates this risk.
Method
Retrospective, observation study of infants, presenting between June 2022 and February 2023 with clinical and biochemical profiles suggestive of CAH and paired measurements of cortisol made by CLIA and LC–TMS.
Results
Three infants (2M, 1F) were noted to have discrepancies in cortisol concentrations measured by CLIA and LC–TMS. The female patient had virilised genitalia. All patients had hyponatremia, hyperkalaemia but remained normoglycemic. Cortisol concentrations were healthy on SDSST analysed by CLIA in two patients, however other biochemical parameters were consistent with a diagnosis of CAH. Samples were therefore reanalysed by LC–TMS and were found to be low. The third patient had low cortisol on SDSST, with a healthy random cortisol measurement. Cortisol measurements by CLAI and LC–TMS are given in Table 1.
Table 1 Cortisol concentrations on baseline and peak samples on SDSST, and random samples measured by CLIA and LC–TMS, and 17-hydroxyprogesterone in three infants with CAH.

Patient (Sex, age)	Baseline cortisol CLIA	Baseline cortisol LC–TMS	Peak cortisol CLIA	Peak cortisol LC–TMS	Random cortisol CLIA	Random cortisol LC–TMS	Random 17-hydroxyprogesterone
M 5 days	635	–	659	–	673	97	>1000
F 7 days	465	36	521	40	–	–	482.6
M 4 months	205	–	253	–	367	91	228

Cortisol and 17-hydroxyprogesterone are reported as nmol/L

Conclusion
Cortisol measured by CLIA is unreliable in infants with very high levels of 17-hydroxyprogesterone, and it's metabolites, secondary to 21-hydroxylase deficiency CAH. Therefore, we recommend cortisol is measured by LC–TMS.

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P83

A critical appraisal of online patient education resources for the management of sick day episodes in adrenal insufficiency

Anna Bradford, A Mason & SC Wong
Department of Paediatric Endocrinology, Royal Hospital for Children Glasgow, Glasgow, UK

Background
Effective management of adrenal insufficiency (AI) during sick day episodes involves adjusting oral glucocorticoid therapy or administering intramuscular injections to prevent adrenal crises. Therefore, educating families of young individuals with AI on emergency management is crucial.
Aim
This study aims to critically evaluate online educational materials related to adrenal crisis management. We conducted a systematic search of online educational resources available on Google and YouTube, as well as a directed search of recognized professional bodies and patient support groups.
Methods
We performed comprehensive searches on Google and YouTube to identify relevant resources. The quality of educational information provided by eligible resources was assessed using a set of specific criteria. Additionally, we evaluated the readability of web pages obtained from Google using the Flesch–Kincaid reading ease score.
Results
We identified a total of 16 patient education resources through Google and 17 through YouTube. More than half (9/16, 56%) of the resources obtained from Google were developed by healthcare providers and researchers, while most YouTube resources (6/17, 35%) were created by patient groups. Out of the 16 web pages, 15 (94%) provided information on adrenal crisis symptoms, 7 (44%) discussed oral sick day dosing rules, and 3 (19%) covered self-injection of hydrocortisone. Nearly half of the eligible web pages (7/16, 44%) had a Flesch–Kincaid score indicating "difficult to read" (30–50). Among the 17 videos, 11 (65%) included information on adrenal crisis symptoms, 6 (35%) discussed oral sick day dosing rules, and 1 (6%) addressed self-injection of hydrocortisone. Most professional bodies and patient support groups offered high-quality patient educational materials targeted towards families of young individuals with AI but these educational materials were not identified through Google or YouTube searches.
Conclusion
The majority of educational resources obtained from Google or YouTube, based on our systematic search, failed to cover several important clinical points for sick day management of AI. Furthermore, nearly half of the resources on Google had a readability level suitable for individuals with tertiary education or higher. It is crucial to better understand the educational needs of families and young individuals with AI in order to develop accessible educational resources.

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P84

Evaluation of early morning cortisol levels compared to short synacthen test to assess adrenal function

Sylvie Bornat[1], Samantha Gorman[2], Emile Hendriks[2], Betty Labeja[2], Karis Reyes[2], Susan Sparrow[2], Ajay Thankamony[2], Loredana Marchovecchio[2], Sue Oddy[3] & Sandra Walton-Betancourth[2]
[1]School of Clinical Medicine, University of Cambridge, Cambridge, UK; [2]Weston Paediatric Endocrinology and Diabetes Clinic, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK; [3]Department of Blood Sciences, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK

Background
The short synacthen test (SST) is commonly used to evaluate the integrity of the hypothalamic–pituitary–adrenal (HPA) axis in children. However, this test is time-consuming, requiring cannulation, several blood samples, and medical observation. Studies in adults have suggested an early morning serum cortisol level could be used to rule out or confirm adrenal insufficiency, reducing reliance on SSTs, however, few studies have evaluated this in children.
Objectives
To define an assay-specific morning cortisol level able to predict adrenal sufficiency in children.
Methods
This was a retrospective single-centre study of SSTs performed at a tertiary paediatric endocrine clinic from January 2020 to May 2023. Tests included were those in children and young people aged 28 days to 18 years old, where an early morning serum cortisol level was collected between 0800 and 1000 hours. Cortisol was measured by Siemens Immunoassay (Centaur and Atellica). A peak serum cortisol of $\geq$450 nmol/L was considered an adequate response to stimulation to rule out adrenal insufficiency. Receiver–operator curve (ROC) analysis was used to determine early morning cortisol levels that could rule out or confirm adrenal insufficiency.
Results
A total of 81 tests were included from 76 children and young people (aged 4 months to 17 years, 43% female). Adrenal insufficiency was diagnosed in 17 (21%) of our patients, based on SST results. ROC analysis revealed that an early morning cortisol of $\geq$292 nmol/L had 100% specificity to rule out adrenal insufficiency, and a level of $<$114 nmol/L could confirm adrenal insufficiency with 100% specificity. By performing SSTs only in young people with early morning cortisol levels between these two cut-offs, in our centre we could avoid 41% of SSTs.
Conclusions
We propose that early morning cortisol levels represent a valid tool for the initial assessment of adrenal function in children and young people with the potential to obviate a substantial number of SSTs.

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P85

Single-centre experience of the use of anastrozole in prepubertal boys with advanced bone age

Eman B Kamaleldeen[1,2], Pooja Sachdev[1] & James Law[1]
[1]Department of Paediatric Endocrinology, Nottingham Children's Hospital, Nottingham, UK, Nottingham, UK; [2]Pediatrics Endocrinology Unit, Department of Paediatrics, Faculty of Medicine, Assiut University, Assuit, Egypt

Background
Aromatase inhibitors block the aromatization of androgens to oestrogen. They are used off-label to delay bone maturation where bone age (BA) is advanced secondary to androgen excess. Side effects include hair loss, headache, decreased appetite, bone pain, drowsiness, and osteoporosis. There is limited data on Anastrozole's safety in paediatrics. We report our experience (Anastrozole 1 mg OD) in 4 pre-pubertal boys with advanced BA.
Case 1
Presented at eight years with paternal concerns about early puberty. On examination A1/P1/G1. Urine steroid profile (USP) and genetic testing confirmed compound heterozygous 21-hydroxylase (21OH) deficiency CAH. Short synacthen (SST) results were 172, 292 and 319 nmol/l at 0, 30 and 60 min, respectively. BA advanced (11.2 at 8.12 years; +3.37 SDS). He was commenced on Anastrozole aged 9.5 years, which was tolerated well.
Case 2
2.9-year-old presented with peripheral precious puberty A1/G2/P2, followed by genetic confirmation of simple virilizing non-salt wasting CAH. Despite cortisol replacement therapy (15.4 mg/m^2 per day) and good adherence, BA continued to advance (Table 1). He was started on Anastrozole & subsequent BA showed marked improvement without side effects.
Table 1 Chronological age (CA) and BA pre- and post-Anastrozole

Year	CA in years	BA in years (SDS)
2017	2.8	6 (+6)
2019	5.1	12.6
2020 (9 months pre)	6.2	12.2
2021 (23 months post)	7.35	12.2 (+5.2)
2022 (34 months post)	8.27	11.98 (+4.0)

Case 3
2-week-old boy presented with salt wasting and was diagnosed with 21OHD CAH. Despite glucocorticoid replacement (14 mg/m^2 per day), BA continued to advance (10.4 at CA 7.1 years). Anastrozole was commenced. After two weeks, he developed severe headaches, which resolved following Anastrozole cessation.
Case 4
6-year-old presented with paternal early puberty concerns (pre-pubertal on examination). Background of MAMLD1 mutation associated with familial non-syndromic hypospadias and early puberty followed by testicular failure. BA was 12.1 at 7.7 CA at Anastrozole commencement. He experienced nausea, tiredness, and hair loss; his medication was stopped for two weeks. He restarted it and tolerated it well.
Conclusion
Two out of four patients experienced significant side effects of Anastrozole which improved on cessation. Careful counselling of side effects is important before treatment initiation.

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P86

An international study of the association between local health care resources and acute adrenal insufficiency events in children with congenital adrenal hyperplasia

Xanthippi Tseretopoulou[1,2], Salma R Ali[1,2], Jillian Bryce[2], Nadia Amin[3], Navoda Atapattu[4], Tania Bachega[5], Federico Baronio[6], Niels H Birkebaek[7], Walter Bonfig[8], Hedi L Claahsen-Van der Grinten[9], Martine Cools[10], Luisa de Sanctis[11], Liat de Vries[12], Heba Elsedfy[13], Christa E Flueck[14], Antony Fu[15], Guilherme Guaragna-Filho[16], Tulay Guran[17], Ayla Guven[18], Sabine E Hannema[19], Violeta Iotova[20], Daniel Konrad[21], Nina Lenherr-Taube[21], Marta Korbonits[22], Nils P Krone[23], Ruth Krone[24], Sofia Leka-Emiris[25], Corina R Lichiardopol[26], Andrea Luczay[27], Renata L Markosyan[28], Inas Mazen[29], Tatjana Milenkovic[30], Klaus Mohnike[31], Uta Neumann[32], Marek Niedzela[33], Anna Nordenstrom[34], Franziska Phan-Hug[35,36], Sukran Poyrazoglu[37], Ursina Probst[38], Tabitha Randell[39], Ana Vieites[40], Gianni Russo[41], Ajay Thankamony[42], Erica van den Akker[43], Judith van Eck[44], Hetty van der Kamp[45], Malgorzata G Wasniewska[46] & Faisal S Ahmed[1,2]

[1]Developmental Endocrinology Research Group, School of Medicine, Dentistry & Nursing, University of Glasgow, Glasgow, UK; [2]Office for Rare Conditions, Royal Hospital for Children & Queen Elizabeth University Hospital, Glasgow, UK; [3]Department of Paediatric Endocrinology, Leeds Teaching Hospitals NHS Trust, Leeds, UK; [4]Lady Ridgeway Hospital, Colombo, Sri Lanka; [5]Unidade de Endocrinologia do Desenvolvimento, Laboratório de Hormônios e Genética Molecular/LIM42, Disciplina de Endocrinologia, Hospital Das Clinicas, Faculdade De Medicina, Universidade de Sao Paulo, São Paulo, Brazil; [6]Department Hospital of Woman and Child, Pediatric Unit, Center for Rare Endocrine Conditions (Endo-ERN), IRCCS – S.Orsola-Malpighi University Hospital, 40138 Bologna, Italy; [7]Department of Paediatrics, Aarhus University Hospital, Aarhus, Denmark; [8]Department of Paediatrics, Technical University Muänchen, D-80804 Munich, Germany and Department of Paediatrics, Klinikum Wels-Grieskirchen, A-4600 Wels, Austria, Munich, Germany; [9]Department of Paediatric Endocrinology, Radboud University Medical Centre, Nijmegen Netherlands; [10]Department of Paediatric Endocrinology,University Hospital Ghent, B-9000 Ghent University, Ghent, Belgium; [11]Regina Margherita Children's Hospital, Pediatric Endocrinology, AOU Citta della Salute e della Scienza, University of Turin, Turin, Italy; [12]Institute for endocrinology and diabetes, Schneider Children Medical Center of Israel, Petah Tiqvah, Israel; [13]Department of Pediatrics, Ain Shams University, 11566, Cairo, Egypt; [14]Pediatric Endocrinology, Diabetology and Metabolism, Department of Pediatrics and Department of Biomedical Research, Bern University Hospital Inselspital, University of Bern, Bern, Switzerland; [15]Department of Paediatrics and Adolescent Medicine, Princess Margaret Hospital, Hong Kong, China; [16]Pediatrics Department, School of Medicine, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil; [17]Marmara University, Department of Pediatric Endocrinology and Diabetes, 34899 Pendik, Istanbul, Turkey; [18]University of Health Science, Medical Faculty, Zeynep Kamil Women and Children Hospital, Pediatric Endocrinology Clinic, Istanbul, Turkey; [19]Emma Children's Hospital, Amsterdam UMC location Vrije Universiteit Amsterdam, Pediatric Endocrinology, Amsterdam, Netherlands; [20]Department of Paediatrics, Medical University-Varna, Varna, Bulgaria; [21]Department of Pediatrics, Division of Endocrinology, University Children's Hospital Zurich, Zurich, University of Zurich, Switzerland; [22]Department of Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University of London, London, UK; [23]University of Sheffield, Sheffield, UK; [24]Birmingham Women's & Children's Hospital, Department for Endocrinology & Diabetes, Birmingham, UK; [25]Pediatric Endocrinology Department, P&A Kyriakou Children's Hospital, Athens, Greece; [26]Department of Endocrinology, University of Medicine and Pharmacy Craiova, Craiova, Romania; [27]Department of Paediatrics, Semmelweis University, Budapest, Hungary; [28]Department of Endocrinology, YSMU, Yerevan, Armenia; [29]Department of Clinical Genetics, National Research Center, Cairo, Egypt; [30]Department of Endocrinology, Mother and Child Health Care Institute of Serbia "Dr Vukan Čupić", Belgrade, Serbia; [31]University of Magdeburg, Magdeburg, Germany; [32]Centre for Chronic Sick Children, Institute for Experimental Paediatric Endocrinology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [33]Poznan University of Medical Sciences, Poland Institute of Pediatrics, Department of Pediatric Endocrinology and Rheumatology, Poznan, Poland; [34]Karolinska University Hospital, Stockholm, Sweden; [35]Paediatric Endocrinology, Hospital EHC-Morges, Morges, Switzerland; [36]Paediatric Endocrinology, Hospital Valais-Sion, Sion, Switzerland; [37]Istanbul Faculty of Medicine, Department of Paediatrics, Paediatric Endocrinology Unit, Istanbul University, Çapa 34093, Istanbul, Turkey; [38]Kantonsspital Winterthur, Winterthur, Switzerland; [39]Nottingham Children's Hospital, Nottingham, UK; [40]Centro de Investigaciones Endocrinológicas "Dr César Bergadá" (CEDIE), CONICET-FEI-División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; [41]IRCCS Ospedale San Raffaele, Milan,Italy, Milan, Italy; [42]Department of Paediatrics, University of Cambridge, Cambridge, UK; [43]Erasmus University Medical Center – Sophia Children's Hospital, dept Pediatric Endocrinology, Rotterdam, The Netherlands; [44]Sophia Children's Hospital, Erasmus Medical Center, 3015 CN Rotterdam, The Netherlands; Leiden University Medical Center, 2300 RC Leiden, The Netherlands, Rotterdam, The Netherlands; [45]Wilhelmina Kinderziekenhuis, Division of Pediatric Endocrinology, Utrecht, The Netherlands; [46]Pediatric Unit, Department of Human Pathology of Adulthood and Childhood, University of Messina, Messina, Italy

Background
The reported occurrence and management of acute adrenal insufficiency–related adverse events in children vary widely between centres and may depend on available resources.
Methods
Real world data from the I-CAH Registry that included a total of 2478 patient years follow-up on 607 children from 44 centres were studied and their association to the results of a health care survey of these centres that enquired about local resources and clinical management policies was investigated. Resources included written and steroid emergency plans with one point assigned for each resource. Of the 44 centres, 32 were from high income countries (HIC) and 12 from low/middle income (LMIC) countries.
Results
The median reported rate of sick day episodes (SDE) per patient year per centre at HIC and LMIC centres was 0.69 (range 0, 6) and 0.49 (0,3) respectively ($P=0.603$). Although the availability of resources for management of adverse events was numerically greater at HIC centres versus LMIC with a median score of 4 (1,7) and 3 (2,6) respectively, this did not reach statistical significance ($P=0.109$). There was no significant association between the availability of resources and the SDE rate in LMIC or HIC centres ($P=0.195$). The use of double dose hydrocortisone was reported more frequently in LMIC vs HIC centres (67% vs 22%, $P=0.005$). For management of adrenal crises, the most frequently reported medications included parenteral bolus hydrocortisone (100% in HIC vs 75% in LMIC, $P=0.003$) and saline solution (97% in HIC vs 83% in LMIC, $P=0.112$). Prednisolone was reported to be used more often in LMIC (13% in HIC vs 42% in LMIC, $P=0.033$). A hospital stay of less than 2 days was reported in 50% of HIC centres vs 8% of LMIC centres ($P=0.041$) while a hospital stay of more than 2 days was reported in 26% of HIC centres vs 70% of LMIC centres ($P=0.001$).
Conclusions
There is no clear association at centres between the level of resources available and the rate of SDE. However, there are differences in the management of adrenal crises and these may reflect local availability of resources.

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P87

A case of 17 α-hydroxylase enzyme deficiency; a rare cause of adrenal insufficiency

Alaa Baioumi[1], Proteek Sen[1], Ann Eggers[2] & Toby Candler[1]

[1]Paediatric Endocrinology and Diabetes Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]General Paediatrics Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK

Background
17 α-hydroxylase enzyme deficiency is a rare condition and is responsible for < 1% of cases of congenital adrenal hyperplasia (CAH). Females present with delayed puberty due to reduced production of sex steroids and males can present with female external genitalia or with various degrees of genital ambiguity.
Case presentation
A 4.5-year-old female – previously fit and well – presented to ED with fever and vomiting for 24 hours. On presentation, she had hypoglycaemia (1.6 mmol/L) with hypokalaemia (2.7 mmol/L) and normal blood pressure (BP). There was no hyperpigmentation with normal female external genitalia. Cortisol was 37 nmol/L at the time of hypoglycaemia and an early morning repeat was 12 nmol/L. The child was started on replacement doses of hydrocortisone. A synacthen test subsequently confirmed primary adrenal insufficiency with a peak cortisol of 25 nmol/L and elevated ACTH (101 ng/L, normal range 7.2 – 63.3). Anti-adrenal antibodies were negative. Other investigations were normal including Renin 7.5 mU/L (5.4–60), 17OHP <0.1 nmol/L, Androstenedione <0.4 nmol/L, DHEA-S <0.3 umol/L, and Testosterone <0.1 nmol/L. Abdominal ultrasound showed normal adrenal glands. Electrolytes have normalised now well. The

urinary steroid profile (USP) confirmed a complete deficiency of 17 α-hydroxylase with elevated corticosterone metabolites and significantly low androstenedione, dehydroepiandrosterone (DHA), and cortisol metabolites. Genetic testing is awaited.
Conclusion
Patients with 17 α-hydroxylase enzyme deficiency commonly present with delayed puberty and / or hypertension and it is a rare form of CAH. We present a case of a child whose hypocortisolism was identified after a period of hypoglycaemia following an intercurrent illness. She was hypokalaemic (consistent with relative mineralocorticoid excess) though she maintained normal BP during the illness and when well. The key to diagnosis was the USP and we wait for genetic testing to identify the causative mutation. The mainstay of management is glucocorticoid replacement as soon as the diagnosis is made and sex hormone replacement at the expected time of puberty. Close monitoring of BP is essential as hypertension is a clinical feature due to elevated levels of 11-deoxycorticosterone (DOC), corticosterone, and 18-hydroxycorticosterone.

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P88

A case report of profound hyponatremia unveiling Addison's disease

Pankaj Agrawal, Ritika R Kapoor, Charles R Buchanan & Ved Bhushan Arya
Kings College Hospital NHS Foundation Trust, London, UK

Introduction
Addison's disease (AD) is a rare endocrine disorder in children, characterized by insufficient production of cortisol and aldosterone due to adrenal gland dysfunction. While electrolyte imbalances, including hyponatremia, hyperkalaemia, can occur in AD, severe hyponatremia is an unusual and challenging complication in children. We present a case of severe hyponatremia in a teenager diagnosed with AD.
Case report
14-year-old boy presented to Emergency Department (ED) with 1-week history of recurrent vomiting, unsteady gait and extreme fatigue. He had previously undergone investigations (including Growth hormone stimulation test, MRI Pituitary) for delayed growth/puberty. In ED he was noted to be ataxic, with no other neurological deficit. He was clinically not dehydrated (heart rate 70–90/min, blood pressure 110/60 mmHg), no hyperpigmentation. His height (149.3 cm) & weight (35.65 kg) were on 1st centile. Investigations revealed very low serum sodium (Na) 95 mmol/L (135–145), normal: Potassium (K) 5.1 mmol/L / blood pH (7.34) and blood glucose (6.3 mmol/L). Urea / full blood count / liver / thyroid profile were normal. CT scan head normal. Random cortisol (23:30 hrs.) 66 nmol/L. Paired plasma (199 mOsm/kg) and Urine Osmolality (308 mOsm/kg) and urine Na (39 mmol/L) suggested renal salt wasting. Suspecting adrenal insufficiency, he was started on intravenous Hydrocortisone (2 mg/kg intravenous (i.v.) every 6 hours) and oral Fludrocortisone (100 micrograms once daily) after taking appropriate blood samples for Aldosterone, Renin, and ACTH. He was managed in High Dependency Unit with i.v. 3% & 0.9% saline. He remained haemodynamically stable, and his Na slowly increased by 8–10 mmol/L per day. He was shifted to the ward after 3 days once his serum sodium came above 130 mmol/L and HC was switched to oral dose. Pending investigations showed Renin of 4813 mIU/L, ACTH 1886 ng/L (0–46), Adrenal Antibodies positive, VLCFA – negative, confirming Addison's Disease. He was discharged home in stable condition on oral HC, Fludrocortisone & Na supplements with sick day management training.
Conclusion
This case highlights the rare and extremely serious presentation with severe hyponatremia in Addison's disease. It emphasises the need for early recognition, timely intervention with electrolyte correction and hormone replacement therapy, which is crucial for successful management.

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Bone 2

P89

Establishing reference interval values of fibroblast growth factor 23 in paediatrics population

Andre O C Chu[1], Isabelle Piec[2,3], William D Fraser[1,2,3], Rachel Dunn[2,3], Amrou Farag[2], Allison Chipchase[3], Jonathan C Y Tang[2,3] & Emma Webb[2,4]
[1]Norfolk and Norwich University Hospital, Norwich, UK; [2]Faculty of Medicine and Health, Norwich Medical School, Norwich, UK; [3]Clinical Biochemistry, Departments of Laboratory Medicine and Departments of Diabetes and Endocrinology, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [4]Jenny Lind Children's Hospital, Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK

Background
Fibroblast growth factor 23 (FGF23) is a key protein in bone homeostasis regulatingserumphosphateand calcitriol ($1,25(OH)_2D_3$) concentrations. Analytical performance and reference ranges of FGF23 assays differ by molecule assayed (intact or C-terminal FGF23) and manufacturer. We aim to establish reference interval values for both cFGF23 and iFGF23 in a paediatric population.
Methods
Written informed consent was taken from children aged 0 to 16 years with minimal past medical history attending a tertiary centre for a planned surgical procedure. Fasting serum and EDTA samples were collected and calcium intake and medical history recorded. Samples were analysed to measure plasma concentrations cFGF23 (Quidel, USA) and iFGF23 (DiaSorin, Italy), alkaline phosphatase, vitamin D, calcium, and phosphate. Unpaired t test was used to compare difference in analyte concentrations between males and females, children with different vitamin D and phosphate concentrations, and daily calcium intakes. Regression analysis was performed to assess change in analyte concentration with age.
Results
Eighty one females (mean age ± S.D., 8.18 ± 4.51) and 130 males (7.34 ± 4.58) were included in the analysis. Plasma cFGF23 was significantly higher ($P = 0.025$) in males (mean ± S.D.,87.1 ± 28.6RU/mL) than females (76.0 ± 17.8RU/mL). iFGF23 was not significantly different ($P = 0.133$) between males (37.3 ± 12.4 pg/mL) and females (34.3 ± 10.2 pg/mL). There is a non-significant downward trend in the concentration of cFGF23 and iFGF23 with increasing age in females (cFGF23:R2 = 0.136,F(1,41) = 6.451,$P = 0.150$; iFGF23:R2 = 0.044,F(1,56) = 2.550,$P = 0.115$), and males (cFGF23:R2 = 0.027,F(1,66) = 1.801,$P = 0.184$; iFGF23: R2 = 0.032,F (1,93) = 3.110, $P = 0.081$). Low total 25(OH)D (vitamin D) concentrations were significantly associated with decreased iFGF23 ($P = 0.020$). Low phosphate concentration was significantly associated with decreased cFGF23 ($P = 0.015$). Neither cFGF23 ($P =$)0.05 nor iFGF23 ($P = 0.61$) values were associated with daily calcium intake.
Conclusion
We report values of cFGF23 and iFGF23 in a paediatric population with minimal past medical history. We have not yet reported reference intervals, numbers being likely to change as we analyse more samples. Of note, we observe sex differences in cFGF23 only, but no significant changes in cFGF23 and iFGF23 with age. The availability of cFGF23 and iFGF23 paediatric reference values will allow a better clinical use of these tests.

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P90

Systematic review of pharmacological and non-pharmacological therapies for prevention and treatment of osteoporosis in Duchenne muscular dystrophy

Sarah McCarrison[1], Shima Abdelrahman[2], Rosaline Quinlivan[3], Richard Keen[4] & Sze Choong Wong[1,2]
[1]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [2]Department of Human Nutrition, University of Glasgow, Glasgow, UK; [3]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, London, UK; [4]Metabolic Bone Disease Unit, Royal National Orthopaedic Hospital, Stanmore, UK

Background
Glucocorticoid treatment is commonly used for Duchenne Muscular Dystrophy (DMD) in young people, but is associated with a high incidence of fragility fractures. This systematic review aims to assess the current evidence for pharmacological and non-pharmacological treatment for osteoporosis in children and adults with DMD, with the goal of guiding future management strategies.
Methods
Three online databases (Embase, Medline, Cochrane Library) were searched for studies that evaluated interventions for treatment or prevention osteoporosis in DMD. The included studies had to report changes in bone mineral density (BMD) Z-scores or fracture incidence.
Results
Seventeen studies were identified, including eleven on bisphosphonate treatment, two on testosterone therapy, one on vitamin D/calcium, one on teriparatide treatment, and two on vibration therapy. Only two randomised-controlled trials were found, one for bisphosphonate (zoledronic acid) with 24-month follow-up and one for vibration therapy with 14-month follow-up. Among the

bisphosphonate studies, four investigated intravenous administration, five oral administration, one intramuscular administration, and one both intravenous and oral administration. Changes in lumbar spine BMD Z-scores ranged from −0.3 to +1.3 with bisphosphonate treatment, from +0.13 to +0.38 with testosterone therapy, +0.9 with vitamin D/calcium, and from −0.2 to 0.0 with vibration therapy. The zoledronic acid trial showed a significant difference of +1.4 standard deviations in lumbar spine BMD Z-scores between the treatment and no treatment groups. Limited information was available regarding the impact of treatment on fracture incidence, although data from the randomised trial of intravenous zoledronic acid showed a lower rate of vertebral fractures in the treatment group (15%) compared to the no treatment group (24%). None of the studies involved a population without prior fractures, and none addressed individuals over 18 years.
Conclusion
This systematic review provides emerging evidence for the effectiveness of bisphosphonate therapy in improving bone density in children and adolescents with DMD. However, there is limited information regarding fracture reduction. The review did not find studies involving individuals without prior fractures or those over 18 years old with DMD. Developing new clinical guidance for osteoporosis in children and adults with DMD will require expert consensus in conjunction with published evidence.

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P91

Developing national consensus on management of osteoporosis in duchenne muscular dystrophy in the transition to adult care within the UK adult NorthStar network

Shima Abdelrahman[1], Sarah McCarrison[2], Rosaline Quinlivan[3], Richard Keen[4] & Sze Choong Wong[2,1]
[1]Department of Human Nutrition, University of Glasgow, Glasgow, UK; [2]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [3]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, London, UK; [4]Metabolic Bone Disease Unit, Royal National Orthopaedic Hospital, Stanmore, UK

Background
Osteoporosis commonly occurs as a result of long-term glucocorticoid use and muscle weakness in individuals with Duchenne muscular dystrophy (DMD), rendering them highly susceptible to fragility fractures of vertebrae and long bones. Existing clinical guidelines for the management of osteoporosis in DMD primarily focus on paediatric management. In particular, management during transition from paediatric to adult care is not clarified in current international guidance.
Objective
A UK working group was set up to establish a national clinical consensus for the management of osteoporosis in adult patients with DMD with focus on transition from paediatric to adult care.
Method
An expert panel comprising of adult and paediatric bone specialists, adult neuromuscular clinicians, and patient representatives was assembled to develop the clinical consensus through a series of online meetings. Focus groups involving patients and their caregivers were organised to gather feedback on their experience and the management of bone health. Systematic and scoping reviews on osteoporosis therapies for DMD, international consensus guidelines for glucocorticoid-induced osteoporosis in adults, and DXA predictions of fractures in DMD were conducted to inform the expert panel. In the initial round, the expert panel proposed areas of clinical care for which consensus statements will be formulated via an online survey. The final consensus statements will be developed using a three-to-four-round e-Delphi technique.
Results
Of the 22 clinicians invited to participate, 19 (86%) provided their suggestions in the first survey round. The suggested areas were categorised into eight main domains, covering various aspects of osteoporosis risk assessment, treatment, and monitoring. The findings from the three literature reviews confirmed the paucity of evidence regarding bone health management in adults with DMD. The results of these reviews and the outcomes of the focus groups were shared with the expert panel in subsequent online meetings before the voting on the consensus statements commences in September 2023. The final clinical consensus is expected to be published in the spring of 2024.
Conclusion
Employing an e-Delphi-based systematic approach, this study endeavours to develop national guidance for managing osteoporosis in adults with DMD in the UK and to guide management during transition.

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P92

Evaluation of MRI screening practices for foramen magnum stenosis in achondroplasia patients at Evelina London Children's Hospital

Huda Elsharkasi[1], Moira Cheung[2], Robyn GilbeyCross[2], Emma Snow[1], Fiona Regan[1] & Alessandra Cocca[1]
[1]Department of Paediatric Endocrinology and Bone, Evelina London Children's Hospital, London, UK; [2]Department of Paediatric Endocrinology, Great Armond Street Hospital for Children, London, UK

Background
Achondroplasia, the most common skeletal dysplasia, carries a highest risk of developing foramen magnum stenosis (FMS), particularly in young children, leading to cervicomedullary compression and potentially fatal outcomes. Early detection of spinal cord changes through routine MRI screening can help reducing the morbidity and mortality in this population. Considering recent evidence, the bone team at Evelina London Children's Hospital implemented an MRI-based scoring system, the Achondroplasia Foramen Magnum Score (AFMS), to diagnose and assess the degree of FMS.
Objectives
Auditing the current practice at Evelina Hospital regarding the timing of neuroimaging screening for FMS in achondroplasia patients. Additionally, to determine if all patients underwent MRI screening for FMS using AFMS.
Method
Data were collected from electronic records at Evelina between 2021 and 2023. Patients whose baseline MRI images were requested and performed outside the hospital were excluded.
Results
A total of 51 children were included, all of whom received baseline brain and spinal MRI screenings for FMS (100% compliance). Among these, 33 patients underwent the MRI while being fed and wrapped, and 18 patients required general anaesthesia. FMS was detected in 44 out of 51 patients (86%) during the screening process. The median age at which baseline MRI was requested was 3 months, ranging from 7 days to 21 months. Notably, three patients had their baseline MRI requested at much later ages (12, 13, and 18 years) compared to the rest of the cohort, whose median age at referral to Evelina services was 27 days, ranging from 1 day to 13 years. The median time between the MRI request and the scheduled date was 30 days, with a range of 6 to 175 days. Only 26 out of 51 (51%) MRI reports included the AFMS.
Conclusion
These findings shed light on the importance of ongoing improvement and standardization of care for this population. This study emphasizes the necessity of standardized protocols for timely MRI screenings, optimized employment of AFMS for consistent reporting, early referral to specialized centres, and prompt management of FMS. These measures aim to reduce potential complications and enhance patient outcomes.

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P93

Hematopoietic stem cell transplantation partially rescued the bone phenotype and prevented upper airway obstruction in a boy with pycnodysostosis: A case report

Alexis Anand Dass Lordudass[1], Rob Wynn[2], Stuart Wilkinson[3], Raja Padilela[1], Amish Chinoy[1] & M. Zulf Mughal[1]
[1]Department of Paediatric Endocrinology & Metabolic Bone Disorders, Royal Manchester Children's Hospital, Manchester, UK; [2]Stem Cell Transplant Unit, Royal Manchester Children's Hospital, Manchester, UK; [3]Department of Paediatric Respiratory Medicine, Royal Manchester Children's Hospital, Manchester, UK

Introduction
Pycnodysostosis (PYCD) is a rare autosomal recessive disorder caused by a mutation in cathepsin K (CTSK) gene resulting in increased bone density. The condition is characterised by short stature, acro-osteolysis of distal phalanges, osteosclerosis with increased bone fragility, dysplastic clavicula, delayed closure of sutures, mandibular hypoplasia, dental crowding and upper airway obstruction, causing obstructive sleep apnoea syndrome (OSAS). We report a child treated with hematopoietic stem cell transplantation (HSCT).
Case report
A12-year-old born to consanguineous parents. Both older brothers with PYCD had significant growth failure, multiple fractures with poor union, and OSAS requiring tracheostomies in early childhood. Eldest brother's final height (FH) was 129.9 cm (SDS: −6.06), and the second brother's FH was 140.5 cm (SDS: −4.43). At birth, he had micrognathia, pansystolic heart murmur and inspiratory stridor. Skeletal survey showed widespread sclerosis. Echocardiography revealed

a small outlet ventricular septal defect. He had pathogenic homozygous variants in the CTSK gene: c.830C>T (*P*.A277V). Due to the severe phenotype, he had a matched family donor stem cell transplant at 9 months of life. Unlike older siblings, he did not develop OSAS symptoms or suffer fragility fractures. He has mild phenotypic features with micrognathia, hypoplastic maxilla, dental crowding, short dystrophic fingernails, and toenails. He has flat-footed gait and generalised joint hypermobility with Beighton score of 7/9. His latest height is 1.35 meters (SDS: −2.2), and weight at 39.9 kg (SDS: −0.28). BMI is 21.89 kg/m^2 (SDS: 1.88). Polysomnogram revealed mild elevation of Apnoea–Hypopnoea Index (AHI) of 1.3 per hour (<1 per hour). Bone age (TW3) was 13.29 years at chronological age 12.36 years. He has radiological signs of acro-osteolysis of distal phalanges. His size-corrected bone mineral density assessed by Dual-energy X-ray absorptiometry was normal: Bone mineral apparent density (BMAD) of the femoral neck SDS: −1.4 and BMAD of lumbar spine SDS: −0.8.

Conclusion

At present, pycnodysostosis treatment is largely supportive and symptomatic management of complications. HSCT in our patient normalised his bone mineral density, improved the linear growth and he did not develop symptoms of OSAS. HSCT should be considered in severe phenotypes of pycnodysostosis as it may potentially attenuate the phenotype.

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P94

From osteogenesis imperfecta to hypophosphataemic rickets; a story of missed or mis-diagnosis

Mohsina Noor Ibrahim, Heera Nand Rathore, Zubair Khoso, Maira Riaz, Versha Rai Lakhani, Mehrunisa Yasir & Saadullah Chachar
National Institute of Child Health, JSMU, Karachi, Pakistan

We report a Pakistani family of three adults and five children affected with same disorder. An 8-year-old boy referred to us for the management of osteogenesis imperfecta according to mother he was not gaining height, increasing head size, and bowing of legs since the age of 2 years. He had dental caries and brittle teeth. Two of his maternal uncles and one maternal aunt were suffering from the same disease; their children also showed similar complaints. A paternal uncle and aunt were also treated as osteogenesis imperfecta. On examination, he was noticeably short for his age and had signs of rickets ilike frontal bossing, wrist widening, chest deformity, rachitic rosary, and genu valgum. So on index of suspicion of rickets further workup was done. His investigations revealed calcium, magnesium, 25(OH)-Vitamin D along with 1,25(OH)2-Vitamin D were normal, PTH was high, his phosphorus level was low along with raised alkaline phosphatase activity. His fractional excretion of urinary phosphorus was high along with raised TRP and TmP/GFR, which were consistent with renal phosphate wasting. His skeletal survey was suggestive of Rickets. Meanwhile, the family was convinced to have a genetic work up. Due to affordability issue, the paternal uncle's genetic work up was sent first. The initial genetic panel for osteogenesis imperfecta was negative. Later on, a panel for rickets was requested which was positive for PHEX gene.Genetic workup of index case revealed a hemizygous pathogenic mutation in Exon 17 of PHEX gene and the pathogenic variant identified was c.1735G>A (p.Gly579Arg), which is associated with X-linked hypophosphatemia. His mother also had the same pathogenic variant on genetic analysis. Other affected family members were found to be positive for the same pathogenic variant. The conventional therapy with phosphorus and calcitriol supplement was started and the patient showed significant improvement. Novel therapy Burosumab is not available in Pakistan.. This case highlights the importance of considering XLH in patients with predominant lower limb involvement along with dental problems. It also emphasizes the significance of thorough history, examination, proper investigation, genetic work up and appropriate management strategies to optimize outcome.

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P95

Unusual presentation of Isolated Hypoparathyroidism in a young adolescent

Pon Ramya Gokul, Jo Blair, Poonam Dharmaraj & Renuka Ramakrishnan
Alderhey Children's hospital, Liverpool, UK

Introduction

Hypoparathyroidism is an uncommon condition in children characterized by hypocalcemia and hyperphosphatemia due to defective synthesis /secretion of parathyroid hormone (PTH), end organ resistance or an inappropriately activated calcium-sensing receptor (CaSR). Clinical symptoms include muscle spasms, stridor, seizures, and syncope. It is rare for a child with this condition to present with cardiac failure at diagnosis. The therapeutic approaches mainly focus on normalizing calcium levels with the use of calcium supplements and active vitamin D. Here, we present an adolescent boy with cardiac failure secondary to isolated hypoparathyroidism.

Case history

A 13-year-old boy, previously fit and well with only a week's history of hand twitching, spasms and feeling breathless while playing football. He presented in a critical condition with respiratory distress and poor cardiac function. There was no significant medical, surgical, or family history and examination did not reveal any signs of ectodermal dysplasia or fungal infection. The patient required ventilation and inotropic support. Initial echocardiogram showed systolic impairment with poor ejection fraction (EF:35%),and a rim of pericardial effusion in a structurally normal heart. Initial calcium levels were significantly low 1.69 (2.15–2.74 mmol/L) with an inappropriately normal PTH level of 2.1(1.1–6.9 pmol/L), low urine Calcium/creatinine and a normal vitamin D level. Bone profile for close family members was normal. Intravenous calcium and Alfacalcidol were administered, resulting in gradual improvement of calcium levels. Additional tests showed a normal autoimmune workup, elevated cardiac markers (high troponin T 6203 ng/L 0–14), NT-pro B type natriuretic peptide levels 11 346 ng/L (<200) and positive adenovirus PCR on nasopharyngeal aspirate sample. The hypoparathyroidism gene panel result was normal. Currently patient is well with a stable calcium level, a low normal PTH and normal cardiac function.

Conclusion

This case highlights an unusual presentation of hypoparathyroidism. Adenovirus infection can lead to cardiac failure but not known to cause parathyroid dysfunction. Hypoparathyroidism seems idiopathic in our patient, and we speculate if the adenovirus infection further contributed to this critical presentation which needed collaboration between the endocrinologist and cardiologist for comprehensive management.

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Diabetes 3

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EarLy Surveillance for Autoimmune type 1 diabetes (ELSA) – paediatric, general population screening in the UK

Shivam Choudhary[1], Lauren Quinn[2], David Stanley[3], Renuka Dias[4], R Rashid[3], J Garstang[6], D Shukla[7], Sheila Greenfield[8], Alex Richter[9] & Parth Narendran[10]
[1]University of Birmingham, Birmingham, UK; [2]Institute of immunology and Immunotherapy, University of Birmingham, Birmingham, UK; [3]Queen Elizabeth Hospital Birmingham,, Birmingham, UK; [4]Department of Diabetes, Birmingham Children's Hospital, UK; INNODIA Principle Investigator, Birmingham Children's Hospital, Birmingham, UK; [5]School of Medicine, Dentistry and Nursing, University of Glasgow, Glasgow, UK; [6]Birmingham Community Healthcare Trust, Birmingham, UK; [7]Clinical Research Lead for Primary Care (West Midlands), Birmingham, UK; [8]Institute of Applied Heath Research, University of Birmingham,, Birmingham, UK; [9]Head of Clinical Immunology Service, University of Birmingham, Birmingham, UK; [10]Institute of immunology and Immunotherapy, University of Birmingham; Department of Diabetes, University Hospitals of Birmingham, Birmingham, UK

Background

Children with pre-symptomatic type 1 diabetes (T1D) can be identified through testing for circulating islet autoantibodies (AAb). Identifying children at risk reduces diabetic ketoacidosis at onset and allows participation in trials aiming to delay disease onset. Teplizumab is the first immunomodulatory agent licensed in the US to delay the onset of T1D by 3 years in individuals at risk; a licensing decision is awaited in the UK. The EarLy Surveillance for Autoimmune diabetes (ELSA) study is exploring the feasibility and acceptability of UK paediatric general population screening.

Methods

The ELSA study runs from July 2022 to August 2024 and aims to recruit 20 000 children aged 3–13 years. Families are invited via social media and through community settings including schools and general practice. ELSA is screening for AAb via dried blood spot (DBS) and subsequent staging via oral glucose tolerance testing. ELSA is exploring the feasibility and acceptability of UK paediatric general population screening.

Results

In total, 6932 children have consented, including 6488 children for home testing and 444 for screening in community settings. Families are principally White European (92%) and 54% have a family history of T1D. Thus far, 3939 kits have been returned and analysed with 3833 children screening negative and 91 screening positive for AAb. Thus far, 5 DBS kits had insufficient sample and 10 blank cards have been returned. On confirmatory AAb testing, 5 children are false positive (7%), 20 are single (27%) and 49 (66%) are multiple AAb positive. One

child at stage 3 was referred immediately into paediatric diabetes clinical service. Of the remaining multiple AAb children, 35 are stage 1, 2 are stage 1 and 11 await staging. All multiple AAb families agreed to confirmatory testing, staging and education and have expressed interest in INNODIA for monitoring.
Conclusion
Social media is an effective route to recruitment for home testing. Community outreach to schools and general practices is underway. Exploring acceptability and barriers to screening are key outcomes for this study. Qualitative interviews will explore the harms and psychological implications of screening on parents.

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Disparities in using an insulin pump to manage Type1 DM Evelina Children's Hospital experience

Eiman Haj-Ahmed[1], Lillian Wiles[2], Michael Cornish[1] & Fiona Regan[1]
[1]Evelina Children's Hospital, London, UK; [2]King's college University, London, UK

Introduction
In recent years there has been a highlight on the inequity of diabetes care and results across the UK. Research needs to be taken into barriers of access to technology for type 1 diabetes in CYP in the UK, specifically looking at provider bias, systemic issues within the health system, and individual and family factors.
Aim of the study
We explored the potential factors that might affect access to technology for children with Type1 diabetes mellitus, including age; ethnicity; language barrier; deprivation and psychological support.
Methodology
A cohort of ten children diagnosed with Type 1 diabetes, cared for by Evelina Children's Hospital between April 2022 to April 2023, declined the offer of insulin pump therapy. We telephoned the families at least six months later to discuss the reasons behind the decision.
Results
Within the group, 60% were male, and 40% were female. 80% were 11–16 years of age. The ethnicities included 40% Black-African, 20% White British children, 10% White background, 10% mixed-White, 10% Black Caribbean and 10% others. Mean HbA1C according to ethnic group was in Black African ($N=4$) 9.87%, White British ($N=2$) 8.3%, White-any other White background($N=1$) 8.60%,mixed White Back African($N=1$)9.40%,Mixed-White and Black Caribbean($N=1$) 8.60%,any other ethnic group ($N=1$)8.40%. Psychological support and access to technology: All patients had access to a psychologist. 60% of patients who declined pump technology had received psychological support. 83.3% of the 60% had attended at least 50% of their psychology appointments. Deprivation and access to technology: It was evident that declining Insulin pump was common in Black-African living in the third most deprived quintile, Followed by White British children living in the second most deprived quintile.
Conclusion
Teenage patients were most likely to decline the offer of insulin pump therapy. This was most apparent in children of black ethnicity, followed by White British children. Those from Black ethnic backgrounds had the highest HbA1c; over half of the patients in this group engaged with psychology. A significant proportion of children declining Insulin pumps live in the third deprivation quintile.

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P98

Abstract withdrawn

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P99

Improving diabetes outcomes using an intensive structured education programme during first year of care after diagnosis

Mark Burns & Vani Balasubrahmanyam
South Tees Hospitals NHS Foundation Trust, Middlesbrough, UK

Introduction
A diagnosis of type 1 diabetes makes a huge impact on the child and family. We believe intensive training in the first-year after diagnosis is crucial in laying a solid foundation to the lifelong management of this chronic condition. To provide this intensive support and drive reduction in HbA1c we started a quality improvement project focussing on the first year of care. Previously all patients were admitted following diagnosis of diabetes for stabilisation and education. They were seen 3 monthly in MDT clinic with variable contacts in between clinics based on need. Our goal was to develop a structured, focussed education programme with more face-to-face contacts and specific areas of education to cover at each visit.
Objectives
Develop and implement a first year of care education pathway to reduce HbA1c at 12 months after diagnosis
Methods
Creation of a first year of care structured education pathway, implementation on 1st July 2020 and analysis of HbA1c at 3 monthly intervals.
Results
There was a significant improvement in HbA1c from 2020 onwards. Mean HbA1c reduced from 60.15 to 54.93 mmol/mol at 12 months post diagnosis. Percentage achieving 48 mmol/mol at 12 months post diagnosis increased from 3.8% to 30% and the percentage of patients above 68 mmol/mol reduced from 30.7% to 6.6% before and after the intervention.
Conclusions
There was a marked improvement in HbA1c outcome from January 2020 onwards. This was prior to the intervention but the period January to June 2020 was affected by the Covid pandemic where many patients could not get the recommended 3 monthly HbA1c check. The difference in HbA1c pre intervention in 2019 and post in 2020 is considerable. There was a nearly 8-fold increase in the number of patients achieving HbA1c <48 mmol/mol and a nearly 5-fold reduction in percentage of patients with HbA1c >68 mmol/mol at 12 months post diagnosis. This has required a significant investment of time and resources to provide this level of care but it has shown clear benefit. We will continue to evaluate the longer-term outcomes for these patients and families and whether these behaviours and results are maintained.

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P100

The impact of COVID-19 and social deprivation on the outcomes of type 1 diabetes in children

Rachel Drage[1], Fareen Ahktar[1], Tim Barrett[1], Ruth Krone[2], Renuka Dias[2], Vrinda Saraff[2], Zainab Mohammed[2], Suma Uday[1,2], Jan Idkoviak[1,2], Lesley Drummond[2], Louise Collins[2], Catarina Leal[2] & Melanie Kershaw[2]
[1]University of Birmingham, Birmingham, UK; [2]Birmingham Women's and Children's Hospital, Birmingham, UK

Introduction
The National Paediatric Diabetes Audit consistently highlights disparity in Type 1 diabetes outcomes with a higher mean HbA1c observed in the most deprived socioeconomic groups. During COVID concerns escalated as the impact of lockdowns on socioeconomic deprivation had potential to inflate pre-existing health divides. Our study aimed to assess care provided and impact of socioeconomic background on diabetes outcomes through COVID in a large tertiary diabetes service.
Method
A retrospective longitudinal study of a tracked cohort of 142 children and young people diagnosed with Type 1 diabetes for a minimum of 12 months, and who remained in the centre's care throughout pre, peri and post COVID periods (45 months). Median HbA1c was compared using English Indices of deprivation, together with records of diabetes care interventions. Statistical analyses comprised Anova (SPSS), *T*-test and Z test.
Results
83% of the cohort were in the most deprived half of the English population. Whilst mean HbA1c did not significantly differ between the most and least deprived clinic quartiles pre covid, those in the least deprived quartile had a significantly lower HbA1c post COVID than the more deprived quartile ($P=0.002$) with an average difference of 9.3 mmol/mol. There was no significant difference in the total number of team, dietitian contacts or education clinics offered. There was more face-to-face contact with the most deprived half of the clinic who saw a smaller reduction in the number of HbA1c measurements during the lockdowns ($P=0.007$). Although the most deprived were significantly less likely to be on an insulin pump pre ($P=0.045$) and post COVID ($P=0.044$), its use was associated with significantly lower HbA1c pre ($P<0.0001$), peri ($P=0.05$) and post COVID ($P<0.01$).
Conclusion
Our report demonstrates that the general trend for improvement in HbA1c in time was attenuated in the most deprived quartile, despite the team being more likely to see those in the most deprived half of the clinic face to face, and the trend to more frequent team contacts across all socioeconomic groups. Future use of technology is key to closing the gap of the impact of socio-economic status on diabetes outcomes.

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P101

Creation of a simple, online 'hello quiz' for diabetes clinics- to help tailor appointments, improve communication, and aid service development

Claire McNamara, Claire Brookes, Ruth Harris, Kirsty Robinson, Jack Sims, Vineeta Joshi & Mark Robinson
Wrightington, Wigan and Leigh Teaching Hospitals NHS Foundation Trust, Wigan, UK

Background
The NCYPDN plan describes a care model where children, young people (CYP) and families '*co-design their care plan during appointments'* and '*have a say in service planning.*' RCPCH 'Voice Matters' notes children want clinicians to '*better understand how we are feeling, to ensure we're involved in our treatment and have the support we need'*. Our clinic experience found some CYP were limited with input and sharing. Communication barriers included time, mood, age, neurodiversity, anxiety, shyness, language and privacy.
Aim
To create a pre-clinic CYP quiz to capture CYP needs and wants, and collate data for service planning.
Method
A 'Hello Quiz', picture based with simple language to maximise accessibility was created using Microsoft Forms. It was offered via QR code or iPad to CYP in the waiting room. Staff immediately viewed results online.
Results
The quiz successfully allowed us to proactively tailor clinic to the CYP's current mood and wishes. There were 64 CYP over 12 weeks, aged <5yrs (5%), 5–10yrs (30%), 11–15yrs (39%), 16yr+(27%) 55% felt happy, 34% ok, 13% fed up, 3% angry and 2% worried. 50% felt good about their diabetes, 33% ok and 16% bad. Wellbeing support was offered: 22% either wanted (5%) or maybe wanted (17%) this; similar to NPDA psychology data (29%). Peer support and a youth worker were requested. 12% of the 11y+ CYP asked for consultation time alone. 16% of CYP wanted and 14% maybe wanted carbohydrate counting help. CYP scored the quiz 4.73/5 for ease, 4.13/5 helpfulness. Google translate was effectively used.
Conclusion
The quiz was easy and helpful, enabling CYP person centred care; hearing their voice for clinic and service planning. Our CYP want to talk about a variety of topics, and need more wellbeing support.
Future
We aim to recruit a Youth Worker for community wellbeing support, have created a Wellbeing Services leaflet, and planned a transition peer support event.

Topics CYP selected to talk about	
Diabetes	22%
Food	20%
Insulin	17%
Holidays	19%
Education/jobs	16%
Sports/exercise	11%
Emotions/wellbeing	8%
Relationships	5%
Drinking/partying	5%
Friendships	2%
Futures	2%
Video games	2%

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P102

Prohormone convertase 1/3 deficiency can be associated with diabetes mellitus in childhood

Rachel Varughese[1], Sasha Howard[2], Gary Butler[3] & Mehul Dattani[1]
[1]Great Ormond Street Hospital, London, UK; [2]William Harvey Research Institute, London, UK; [3]University College London Hospital, London, UK

Prohormone convertase 1/3 (PC1/3) deficiency is rare, caused by homozygous or compound heterozygous mutations in the PCSK1 gene. PCSK1 encodes a serine protease important in cleavage of several proneuropeptides and prohormones. Despite a variety of known endocrine associations, paediatric diabetes mellitus is rare, described only once before. Previous understanding was that biological activity of elevated proinsulin (<5% of the activity of insulin) confers protection from diabetes mellitus in childhood, and that diabetes emerges in adulthood through B-cell exhaustion. We present two cases of PC1/3 deficiency with diabetes mellitus onset in childhood. The endocrine manifestations were very similar across the two and are summarised in Table 1.
Patient 1
Patient 1 was born at term to consanguineous parents (first cousins). Severe malabsorption from week1 required TPN until 7 months old. At 8.5years, he had marked acanthosis, and an OGTT revealed impaired glucose tolerance, with elevated fasting insulin (54.1 mU/L = 390 pmol/L) and peak glucose 9.7 mmol/L. Insulin therapy led to hypoglycaemia, so management focussed on metformin/-dietary changes. Exome sequencing revealed a novel homozygous PCSK1 nonsense mutation (p.R391*) in the catalytic domain.
Patient 2
Patient 2 was born at term to 'distantly related' parents. Significant diarrhoea from week2 required TPN until 7 months old. He developed diabetes mellitus at 11.5years. Insulin therapy prompted recurrent hypoglycaemias leading to challenging glycaemic control, unsuccessful metformin trial and eventual cautious insulin reintroduction.
Table 1

	Patient 1	Patient 2
Hypothyroidism	Yes-1.5y	Yes-5y
Hypogonadotrophic-hypogonadism	Yes	Yes
Hyperphagia	Yes-4y	Yes-3y
Obesity	Yes-4y-persisted	Yes-5y-resolved in adolescence
Diabetes insipidus	Partial-5y	Partial-4y
Growth hormone deficiency	Yes-8y-GH commenced, coinciding with diabetes mellitus	Yes-7y-treatment delayed due to good height velocity, and then poor glycaemic control
Cortisol deficiency	Yes-6y	Yes-7.5y
MRI Pituitary	Small anterior pituitary, decreased posterior pituitary signal	Normal anterior pituitary, absent posterior pituitary
Final height	−0.485	−1.42
Current weight z-score	+4.39	+0.16

Key Learning:
- Diabetes mellitus in childhood is possible in PC1/3 deficiency, warranting assessment in known cases
- Diabetes phenotype in both included:
  1 A mixed picture of insulin insensitivity and insulin deficiency
  2 Recurrent hypoglycaemic episodes with insulin (suggesting preservation of insulin sensitivity)
  3 Swinging hypo-/hyperglycaemia (theorised to be related to delayed effects of proinsulin, which has a five-fold longer half-life than insulin).

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P103

Dietary intervention for the management of adolescent type 2 diabetes mellitus: A systematic review

Alisha Bhanot[1,2], Katherine Hawton[3,2], Rachel Perry[2], Julian Hamilton-Shield[4,3] & Toby Candler[3,2]
[1]Southmead Hospital, North Bristol NHS Foundation Trust, Bristol, UK; [2]University of Bristol, Bristol, UK; [3]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [4]NIHR Biomedical Research Centre (Nutrition), University of Bristol, Bristol, UK

Introduction
Despite an increasing incidence of adolescent type 2 diabetes mellitus (T2DM) with its associated morbidities and poor long-term prognosis, there remains uncertainty in its management. The National Institute for Health and Clinical Excellence (NICE) currently recommends initial lifestyle modifications alongside pharmacology management with metformin. Despite being shown to be effective in adults, little is known about the impact of lifestyle interventions, in particular dietary interventions, in adolescents with T2DM. The aim of this systematic review is to provide up-to-date evidence on the impact of dietary interventions in adolescents with T2DM to inform clinical practice.
Methods
The databases Embase, MEDLINE (via OVID), CENTRAL via Cochrane library, Web of Science and CINAHL were searched from January 2000 to May 2023 for studies involving dietary intervention in children under 19 years with T2DM. All study types were included. Titles and abstracts were screened, with 10% reviewer crossover, using Rayyan. All full-text articles and risk of bias assessments were assessed independently by two reviewers. The primary outcome was glycaemic control measured by HbA1C.
Results
Of 8352 search results, only four papers met inclusion criteria, with 28 children undergoing very low energy/calorie diets. Three studies were observational with two utilising matched controls, and the other a feasibility study in a small sample with no control group. No randomised control trials (RCTs) were identified. Results showed certain dietary interventions, such as carbohydrate counting and limiting high fat foods, achieved weight loss, significantly reduced HbA1C and

beneficial changes to baseline pharmacological treatment. However, only one study reported longer term follow up and the effects on HbA1C were not sustained over 24 months, despite an improvement in BMI remaining.
Discussion
Our results show limited evidence, with a lack of robust clinical trials to support the effectiveness of dietary interventions in the management of T2DM in adolescence. Given the increasing incidence of adolescent T2DM, evidence of benefit in adulthood and encouraging short-term results from initial trials during adolescence, it is imperative that RCTs with larger sample sizes and longer term follow up are undertaken to determine the true effectiveness of dietary interventions on outcomes in adolescent T2DM.

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P104

Sodium point of care testing at home in diabetes insipidus: A case report

Anika Sharma[1,2] & Hoong-wei Gan[3]
[1]Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; [2]Homerton university Hospital Trust, London, UK; [3]Great Ormond Street Hospitalfor Children NHS Foundation Trust, London, UK

Patients with central diabetes insipidus (CDI) and concurrent hypothalamic adipsia can experience significant sodium fluctuations requiring prolonged, recurrent hospital admissions and frequent serum sodium testing. We report a case of a 13-year-old male with adipsic CDI where the use of a point of care sodium analyser at home to titrate fluid and desmopressin administration resulted in stabilisation of his serum sodium, prevention of unplanned hospital admissions and improvement in his quality of life. Following a diagnosis of a low grade optic pathway glioma at 3 years of age, he was treated with multiple lines of chemotherapy (carboplatin/ vincristine/ cyclophosphamide/ cisplatin, thioguanine/ procarbazine/ CCNU/ vincristine (TPCV), bevacizumab/ irinotecan) as well as multiple neurosurgical procedures (two ventriculoperitoneal shunt insertions, four shunt revisions and two debulking surgeries). As a result of both the tumour and treatment he developed panhypopituitarism with adipsic CDI. Due to this, he had frequent fluctuations in serum sodium with multiple admissions for hyponatremia and hypernatremia. The year prior to starting the iSTAT machine he spent 155 days in hospital and sustained hypoxic brain injury due to severe dehydration secondary to hypernatraemia (peak serum sodium 170 mmol). To prevent future admissions, he required community blood testing three times a week to guide titration of fluids and desmopressin. We finally obtained funding for an iSTAT-1 machine at home, a point of care serum sodium analyser which gives results in 2 min with <100 µl of blood. In the year following the introduction of the iSTAT machine, the patient had no unplanned admissions, and stable sodium levels tightly controlled by fluid titration alone. This resulted in an estimated cost-saving of >£450 000 per annum. This case highlights how point of care sodium testing at home in patients with adipsic CDI can reduce hospital admissions, save healthcare costs and improve the long-term quality of life of brain tumour survivors.

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P105

Management of diabetic ketoacidosis in 0 to 16 years presenting to the Southern Health and Social Care Trust between January 2020 and September 2022

Shilpa Shah, Shane McVeigh, Rebekah Murphy, Asma Abdin & Sarinda Millar
Southern Health and Social Care Trust, Belfast, UK

Introduction
Diabetic Ketoacidosis is a life threatening emergency. BSPED has updated their guideline with changes in the fluid management (bolus dose for shock, de-escalate early use of inotropes, percentage dehydration in moderate DKA and maximum weight)
Aims
To determine the clinical features and outcome of new presentations of DKA in 0–16 year age range and audit fluid management
Methods
Patients 0-16 years presenting as new diagnosis of DKA over 18 months were recorded and management analyzed.
Results
35 patients with DKA within 132 new diagnosis of type 1 diabetes in 0–16 Mean age 8 ½ years; youngest 16 months 18 male 17 female 20 self-presented to Emergency Department, 1 to ward, 14 GP referrals 16 Severe, 5 Moderate, 14 Mild DKA Paediatric Intensive Care admission in 6 patients. 15 patients had complications, hypokalaemia in 11 patients Average length of stay in hospital was 4.1 days Signs of Shock noted in 12 patients Fluid bolus appropriately administered in 33 patients. 1 had a 20 mL/kg bolus given when not shocked, 1 had a 10 mL/kg bolus when in shock and in severe DKA All 35 patients had percentage dehydration estimated appropriately
Maintenance fluids
Maintenance fluids were calculated appropriately in 30 patients. Of the 4 patients with inappropriate maintenance fluids, 1 had wrong estimated weight 3 did not get 10/kg bolus subtracted Dose of Insulin dose $n=34$ as one patient went to PICU prior to starting insulin infusion due to difficult access 29 started with 0.05 U/kg per hour and 5 had 0.1 U/kg per hour. 3 patients subsequently had insulin increased from 0.05 to 0.1 U/kg per hour. The average duration on the DKA protocol was 21 hours with a range of 8 hours to 2 days and 18 hours
Conclusions
A third of all cases of new diagnosis presented in DKA Male to Female ratio almost equal Just under half were severe DKA Less than 20% required PICU Fluid management was appropriate in over 90% of the cases with commonest error being maintenance fluid. Hypokalemia was the commonest complication and noted in 30% of all DKA despite appropriate fluid management There were cerebral edema or mortality

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P106

'Getting it right from the start' – A quality improvement project to reduce inequalities in access to diabetes related technology

Rachel Whittaker & Julie Smith
Derbyshire Children's Hospital, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK

Background
The National Paediatric Diabetes Audit has identified inequalities in diabetes care. Children and young people (CYP) with Type 1 Diabetes Mellitus (T1DM) from both ethnic minority backgrounds and deprived areas are more likely to have reduced access to diabetes technologies and a higher HbA1c. In our service there was an inconsistent approach to the initiation of Continuous Glucose Monitoring (CGM) and use of insulin pumps. The introduction of a standardised approach to the use of technology aimed to reduce inequalities, eliminating unconscious bias and improve diabetes technology access and outcome (HbA1c).
Methods
A Plan, Do, Study, Act (PDSA) cycle was used to introduce a patient pathway 'Getting it right from the start'. It was agreed at a team away day, ensuring team engagement. It started at diagnosis, during inpatient care. If eligible (less than 5 years of age or with a learning difficulty) real time CGM (rtCGM) was commenced immediately, all other patients were offered Freestyle libre (FSL). Each clinic appointment in the first 6 months of diagnosis had clear objectives. Those eligible, were offered an insulin pump and added to the waiting list. CGM education was integral to the consultation. The HbA1c was assessed after 6 months of diagnosis.
Results
The whole team adopted the pathway and patients with T1DM were commenced on CGM (rt or FSL) at diagnosis. No patient declined. In 11 out of 12 patients less than 12 years of age, an insulin pump was agreed. In 1 out of 6 patients greater than 12 years of age, a pump was agreed due to persistently high HbA1c. At 6 months, HbA1c before implementation (January to June 2021) the mean was 52 mmol/mol and median 55 mmol/mol and after implementation (January to June 2022) the mean was 50 mmol/mol and median 51 mmol/mol.
Conclusion
The use of quality improvement methodology enabled a consistent approach and whole team engagement. The pathway has resulted in ubiquitous access to CGM from diagnosis and improved access to insulin pumps. A structured approach to diabetes education improves outcome in CYP newly diagnosed with T1DM.

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P107

Levelling the Levemir: Are we prescribing too much long-acting insulin to children at diagnosis?

Henry Gann[1], Joely Clarke[2], Eirini Mitropoulou[3], Susannah Deamer[1], Edward Andrews[1] & Emma Knight[3]

[1]Department of Paediatrics, University Hospitals Dorset, Poole, UK; [2]Department of Paediatrics, Dorset County Hospital, Dorchester, UK; [3]Department of Paediatrics, Queen Alexandra Hospital, Portsmouth, UK

Introduction
National guidance from the Association of Children's Diabetes Clinicians (ACDC) recommends starting children with newly diagnosed type 1 diabetes mellitus on a total daily insulin dose of 0.5–0.75 iU per kilo per day (kg/d). This equates to a basal insulin dose of between 0.25–0.375 iU/kg per day. Local practice suggested many patients required a significantly smaller starting dose of basal insulin.
Aim
To evaluate the dose of Levemir at first clinic review with that recommended by ACDC guidelines.
Method
A retrospective service evaluation collecting data of paediatric patients presenting to 3 district general hospitals between 2020 and 2022. Basal insulin prescription recommended at diagnosis was compared against the dose at first clinic review. Data were obtained from patients with a new diagnosis of type 1 diabetes. Data collection included: Patient demographics, Levemir dosage at diagnosis, Levemir dosage at first clinic visit and weights.
Results
We collected data on 142 patients. 34 patients were excluded for incomplete data or alternative basal insulin.

Age group (years)	Number of patients	Median (IQR) Levemir dose at first clinic (iU/kg/d)	Mean(±95%CI) change in Levemir dose: diagnosis vs first clinic (iU/kg/d)
1–3	2	0.087 (0.009)	−0.163±0.017
1–3 DKA	8	0.185 (0.316)	+0.084±0.094
4–6	13	0.106 (0.085)	−0.109±0.033
4–6 DKA	6	0.126 (0.093)	−0.127±0.032
7–9	14	0.193 (0.098)	−0.064±0.054
7–9 DKA	18	0.220 (0.082)	−0.050±0.047
10–12	14	0.223 (0.089)	−0.093±0.044
10–12 DKA	14	0.252 (0.107)	−0.045±0.042
13–15	6	0.268 (0.112)	−0.101±0.074
13–15 DKA	13	0.344 (0.131)	−0.045±0.081

(DKA: Diabetic Ketoacidosis)
Mean dose of Levemir at first clinic All ages 0.224 iU/kg/d (95%CI±0.022)
Conclusion
The median doses of Levemir at first clinic review are below the ACDC recommended starting doses of basal insulin. There was a mean reduction in Levemir at first clinic review in all ages, except for those children aged 1 to 3 in DKA. These data suggest the current ACDC recommended starting dose of basal insulin may be too high. More research is required to establish a personalised appropriate starting dose of long-acting insulin.

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Diabetes 4

P108

The impact of COVID-19 and ethnicity on the outcomes of type 1 diabetes in children

Fareen Akhtar[1], Rachel Drage[1], Tim Barrett[1], Ruth Krone[2], Renuka Dias[2], Vrinda Saraff[2], Zainab Mohammed[2], Suma Uday[2,1], Jan Idkowiak[2,1], Lesley Drummond[2], Louise Collins[2], Catarina Leal[2] & Melanie Kershaw[2]
[1]University of Birmingham, Birmingham, UK; [2]Birmingham Women's and Children's Hospital, Birmingham, UK

Background
The National Paediatric Diabetes Audit consistently highlights disparity in Type 1 diabetes outcomes across different ethnic groups. During COVID concerns escalated as the impact of lockdowns on ethnic minority groups had potential to inflate pre-existing health divides. This study aims to consider if COVID-19 differentially impacted children with Type 1 diabetes in different ethnic groups (White, Black, Asian, Mixed, Other).
Method
A retrospective longitudinal study of outcome in a tracked cohort of 142 children and young people diagnosed with Type 1 diabetes for a minimum of 12 months, and who remained in the centre's care throughout the pre, peri and post COVID periods (45 months) together with records of specific diabetes care interventions. Statistical analyses comprised Anova (SPSS), *T*-test and Z test.
Results
142 patients (mean age 11.1 years) were included, 12% required interpreters. 61%($N=87$) were non-white. Mean HbA1c did not differ between ethnic groups pre, peri and post COVID or longitudinally. More frequent HbA1c measurements were taken from children of Asian and Black ethnicity pre COVID ($P=0.003$) but not peri and post COVID. Children from Black and Asian ethnic minorities had a mean 3–3.9 mmol/moL higher HbA1c throughout compared with white children (non-significant). Black minorities had the greatest drop in the total number of diabetes care contacts, having had the highest numbers pre COVID compared to white ($P=0.011$) and Asian children ($P=0.036$). Children needing interpreters had significantly more clinic appointments offered (pre and peri COVID $P<0.0001$, mean 54 vs 43, and 57 vs 40 contacts respectively) and more HbA1c readings taken peri-COVID ($P=0.01$), thus were seen more often face-to-face. No differences were seen in the BMI Z score, dietetic or educational contacts. There was no significant difference in diabetes therapy between ethnic groups, but interpreter requirement significantly reduced the likelihood of insulin pump therapy pre ($P=0.014$) and post ($P=0.024$) COVID.
Conclusion
There was no change in HbA1c between ethnic groups pre, post or peri-COVID. Differences were seen in care delivery in Asian and Black ethnic minorities, and those requiring interpreters, but this did not appear to adversely affect outcomes and may have been protective.

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P109

What do young people with type 1 diabetes really think about the new advances in diabetes technology?

Sarinda Millar, Kathryn Parker & Niamh McConville
Southern Health and Social Care Trust, Newry, UK

Background
The rapid progression in diabetes related technology should in theory make it easier to self-manage diabetes. Previous studies have shown an improvement in glycaemic control and reduced disease burden. However young people show less sustained use of technology, with potential barriers hypothesised as body image difficulties, perception of standing out from peers and not wishing to have devices attached. This study aims to explore the reasons young people choose not to wear glucose monitoring devices, and understand the daily impact on those who do choose to wear them.
Method
Young people aged 12–18 years with type one diabetes attending the Southern Health and Social Care Trust were invited to complete a validated questionnaire, either online or in person while attending outpatient clinic.
Results
95 young people completed questionnaire, average age 14.4 years. 9.5% young people currently only use a glucometer. 1 young person has never trialled any device. The reasons identified for discontinuing use were dislike of having a device attached, the impact of others seeing this, concerns with accuracy and skin reactions. 47% used freestyle libre 2, 34% used Dexcom G6, and the remainder used a guardian link or alternative. For those using these devices improvements in independence (92%) and confidence (86%) were reported. There was also a positive impact on diabetes management in school (96%) and when with friends (92%). 72% reported worry about how diabetes could affect them in the future. 38% of young people felt their current diabetes management would impact on their future. 28% would like more education to reduce potential complications.
Conclusions
Sustaining use of diabetes related technology remains challenging for adolescent population. Reasons identified were dislike of having a device attached, the impact of others seeing this, concerns with accuracy and skin reactions. Concerns regarding the potential impact of diabetes on future health are reported, but doesn't correlate with a wish for further education. A focus group with young people is planned to further explore the themes identified from questionnaire results. Also a validated questionnaire and focus group for parents and carers will explore the impact on parents and carers.

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P110

Assessing diabetic ketoacidosis management: an audit of clinical practices at bristol royal hospital for children

Alaa Baioumi[1,2] & Toby Candler[1]
[1]Paediatric Endocrinology and Diabetes Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]Paediatrics Department, Ain Shams University, Cairo, Egypt

Background
Approximately 1/3 of children newly diagnosed with type 1 diabetes (T1D) present with diabetic ketoacidosis (DKA). Despite the progress made in managing T1D, DKA continues to pose a substantial risk for existing and new patients with T1D. The British Society for Paediatric Endocrinology and Diabetes (BSPED) published guidelines for the management of DKA in 2021 and this protocol was adopted by Bristol Royal Hospital for Children.
Methodology
Retrospective data collection for children presenting with DKA from 01/01/2022 to 31/12/2022 was done and compared to 23 audit standards. They included correct identification of DKA, fluid management, giving insulin as per the BSPED protocol, electrolytes monitoring, investigations for the newly diagnosed patients, and the timing of medical reviews.
Results
29 patients were diagnosed with DKA ($n=13$ males and $n=16$ females). Their age ranged between 0.8 – 15.4 years with a mean age of 10.7 years. 28 (96.6%) had a correct diagnosis of DKA so were included in the results. 12 patients presented in severe DKA (43%), 7 were in moderate DKA (25%), and 9 were in mild DKA (32%). 18 patients (64.3%) were newly diagnosed with T1D. One patient presented following a cardiac arrest at home. 9/23 (39%) audit criteria achieved full compliance with audit standards which included correct classification of the degree of DKA, initial fluid bolus, deficit and maintenance fluid calculation, hourly blood glucose, 1–2 hourly ketone monitoring, initial U&E, prescribing of potassium in the IV fluids and insulin infusion rate. Medical reviews 2 hours after starting treatment were fulfilled in 96% of patients and starting insulin within 1–2 hours was achieved in 93%. Criteria that needed improvement included, documenting the initial GCS (75%), following it up at regular intervals (64%), and checking 4 hourly U&Es (61%).
Conclusion
Particular focus needs to be made to ensure timely checking and documenting GCS, 4 hourly U&Es, and hourly fluid balances. Therefore, a patient safety message was circulated to all staff, highlighting the areas that needed improvement. Additionally, further training sessions were conducted to enhance DKA management skills, focusing on various scenarios that were identified as problematic during the audit.

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P111

Impact of socio-economic deprivation on the management of type 1 diabetes in children

Haris Shoaib, Shahida Ahmed, Ruth Francks & Sanjay Rawal
Basildon & Thurrock University Hospital, Basildon, UK

Aims
To assess the impact of socio-economic deprivation on access to diabetes technology, specifically insulin pumps, and its outcome in children with type 1 diabetes.
Methods
We designed a retrospective, observational single-centre study of patients attending the paediatric unit at Basildon & Thurrock University Hospital (BTUH). The study included all patients actively receiving diabetic care as of April 2023, including those with access to insulin pumps between January 2012 and April 2023, with their HBA1c values assessed before and after insulin pump treatment. Deprivation quintiles were calculated using the English Indices of Deprivation 2019. Statistical significance was calculated via unpaired *t*-tests, one-way ANOVAs and chi-squared tests.
Results
Included in the study were 243 children with a mean age of 13 years, of which 117 were males (48%). Of this caseload, 48 children had active access to insulin pumps with a mean deprivation quintile of 3.15 (s.d. 1.44). Quintile 1 identified the most deprived populations and quintile 5, the least deprived. The insulin pumps were most accessible for children in the least deprived quintile compared to those in the most deprived quintile (31% vs. 10%; $P<0.01$). Within the caseload, following initiation of treatment, children in the most deprived quintile had the highest mean HBA1c values compared to the lowest values in the least deprived quintile [67.83 (s.d. 24.72) vs. 51.64 (s.d. 9.45); $P=0.027$]. HBA1c outcomes were available for 35 children using pumps, with no statistically significant link to deprivation ($P=0.348$). Children of white ethnicity had the highest use of insulin pumps compared to any other ethnicity (88% vs. 12%, $P<0.0001$).
Conclusions
Inequalities in access to diabetic technology still exist, with children in the least deprived quintile and those of white ethnicity experiencing greater access to technology. Children from all deprivation quintiles experienced positive glycaemic control with technology use, suggesting improving access to technology may reduce glycaemic disparities in deprived populations. Owing to strict criteria from NICE and integrated care boards for approval of diabetic technology, the most deprived populations are disadvantaged by their lack of exposure, awareness and engagement. Further research is yet required to address these health inequalities.

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P112

An unusual case of hyperosmolar hyperglycaemic state

Rhiannon McBay-Doherty & Noina Abid
Royal Belfast Hospital for Sick Children, Belfast, UK

Background
We present an unusual case of Hyperosmolar Hyperglycaemic State (HHS). A 9 year old girl with complex neurodisability due to HIE, presented with HHS twice within one year. Despite this, she has not yet developed diabetes mellitus and moreover, a raised HbA1c has since normalised.
Clinical presentation
In January 2022 she presented with lethargy and increased wet nappies. She had had two recent minor illnesses and had an acutely infected scalp wound on examination. She was severely dehydrated with a weight loss of 1.7 kg (<0.4th centile). Her GCS was 9/15. Her capillary blood glucose (BG) was 39.4 mmol/L and ketones 0.9 mmol/L. A venous blood gas showed pH 7.32 and bicarbonate 28.7 mmol/L. Initial investigations demonstrated elevated serum osmolality (418 mOsm/kg), severe hypernatraemia (sodium >180 mmol/L) and an AKI. In December 2022 she had been unwell with a diarrhoeal illness and became severely dehydrated. She developed a LRTI, later confirmed Influenza A, and had a respiratory arrest at home requiring CPR and intubation. On attendance her BG was >29 mmol/L and serum sodium 177 mmol/L with mild ketonaemia.
Management
On both occasions she was admitted to PICU for IV fluid and electrolyte management as per ACDC/BSPED HHS guideline with gradual normalisation of her sodium and glucose. Subcutaneous insulin was administered on her first episode only. Further investigations included a satisfactory urine osmolality, negative pancreatic autoantibodies and slightly high C-peptide and Insulin when normoglycaemic. Her HbA1c was 38 mmol/mol during her first episode but 46 mmol/mol on her second. This was repeated post discharge and had fallen to 31 mmol/mol. Her outpatient plan is to performs twice weekly BG monitoring with increased frequency during periods of illness and to seek medical review if hyperglycaemic.
Discussion
HHS is a triad of severe hyperglycaemia >33.3 mmol/L, increased serum osmolality >320 mOsm/kg and severe dehydration without marked ketoacidosis. HHS can be triggered by illness and is known to occur in children with diabetes mellitus, this may be undiagnosed before presentation. This case is of particular interest as it is still not clear whether she is progressing towards a diagnosis of Type 1 or 2 diabetes eighteen months post her first presentation of HHS.

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P113

Regional audit on presentation in diabetic ketoacidosis(DKA) at the manifestation of type1 diabetes in children and young people within Yorkshire and Humber region (YH)

Astha Soni[1], Shaimaa Sahmoud[2,3], Geraldine Lennon[4], Sunil Bhimsaria[5], Lovlin Joseph[6], Anuja Natarajan[7], Shaun Gorman[8], Stephanie How-Yaw[9], Nasar Alaber[10], Verghese Matthew[11], Fiona Campbell[12], Victoria Hemming[13], Imran Bashir[14], Elizabeth Baker[15], Nandita Danda[16], Madhavi Madhusudhana[17], Wendy Watts[18], Emma Savage[12] & Sanjay Gupta[11]
[1]Sheffield Childrens Hospital NHS Foundation Trust, Sheffield, UK; [2]Yorkshire and Humber Deanery, Hull, UK; [3]Suez Canal University, Egypt, Egypt; [4]Airedale NHS Foundation Trust, Airedale, UK; [5]Barnsley Hospital NHS Foundation Trust, Barnsley, UK; [6]Doncaster and Bassetlaw NHS Hospitals Foundation Trust, Bassetlaw, UK; [7]Doncaster and Bassetlaw NHS Hospitals Foundation Trust, Doncaster, UK; [8]Beadford Teaching Hospitals NHS Foundation Trust, Bradford, UK; [9]Calderdale and Huddersfield NHS Foundation Trust, Calderdale, UK; [10]Harrogate and Distrcit NHS Foundation Trust, Harrogate, UK; [11]Hull University Teaching Hospitals NHS Trust, Hull, UK; [12]Leeds Teaching Hospitals NHS Trust, Leeds, UK; [13]Mid Yorkshire Hospitals NHS Trust, Dewsbury, UK; [14]The Rotherham NHS Foundation Trust, Rotherham, UK; [15]York and Scarborough Teaching

Hospitals NHS Foundation Trust, York, UK; [16]North Linconshire and Goole NHS Foundation Trust, Grimbsby, UK; [17]North Linconshire and Goole NHS Foundation Trust, Scunthorpe, UK; [18]York and Scarborough Teaching Hospitals NHS Foundation Trust, Scarborough, UK

The incidence of children presenting with DKA at diagnosis has been on the rise worldwide[1]. 25.8% of newly diagnosed children had DKA at diagnosis according to the NPDA report (2020/21). 34% of newly diagnosed children in the Yorkshire and Humber(Y&H) region presented in DKA[2]. Delayed presentation due to lack of awareness is a likely cause for that.

Aim

To review the presentations of DKA at diagnosis in the YH region. Methods: Prospective regional audit included 15 diabetes units in YH area. The audit was coordinated by the YH diabetes network. Prospective data was collected over one year (January 2022–December 2022). Results: There were 334 newly diagnosed type I diabetes children, 137 (41%) presented with DKA, 54 (16.7%) presented with severe DKA. 107 (78%) of children who presented in DKA contacted health care professionals within the last 2 weeks. 92/107 (85.9%) were diagnosed at first contact. The most contacted health care professional was GP by 75 (70.1%) families. The mean duration of symptoms 17(8.9–45) days. The most common symptoms were polyurea and polydipsia in 127 (92.7%), followed by weight loss and fatigue in almost 75% of children. Only 19 (13.9%) of families suspected diabetes before contacting HCP and 20 (14.6%) of them knew family members diagnosed with diabetes.

Conclusion

Many children presented with DKA at diagnosis despite longer duration of diabetes symptoms and not all of them were diagnosed at first contact with HCP. This data highlights the importance of raising awareness about type 1 diabetes within communities and primary care.

Table 1 Demographics

Gender	Boys	76 (55.5%)
	Girls	61 (44.5%)
Mean age at diagnosis (Y)		9+1.88
Ethnicity	White British / any other white	108 (85%)
	Asian	10 (7.9%)
	Black, Caribbean, or African	2 (1.6%)
	Mixed ethnic group	3 (2.4%)
	Others	4 (3.1%)
Has siblings *n* (%)		100 (73%)

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Breaking down the barriers in allergic contact dermatitis to continuous glucose monitors

Nina Mann[1], Tanya O. Bleiker[1] & Julie Smith[2]
[1]Dermatology Department, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK; [2]Paediatric Department, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK

The National Institute for Health and Care Excellence (NICE) recommends continuous glucose monitoring devices (CGMDs) for all adults and children with Type 1 diabetes mellitus (T1DM). Automated technologies such as hybrid closed loop (HCL) systems can improve outcomes and quality of life for patients, their families and carers. There have been increasing reports of cutaneous allergic reactions to medical devices, including CGMDs, in the literature. These reactions are mostly to the sensor of the CGMD, which is held in place on the skin with adhesive. The commonest allergens identified in these devices are the acrylates. Identifying allergens in medical devices is a major problem and is not a legal requirement of manufacturers. This complicates the identification and patch testing of potential allergens making it difficult to recommend an alternative device. Should allergic contact dermatitis (ACD) develop, individuals may have to stop CGMDs with a negative impact on quality of life and diabetes control. We report two cases of ACD to CGMD sensors in children with T1DM, who were using HCL system, where the skin reaction was prevented by the placement of a solid hydrocolloid barrier between the adhesive on the sensor and the skin. A child aged 14 developed a reaction to HCL, Medtronic 640G. She had previously used the Freestyle Libre 1 but discontinued use after 10 months due to severe ACD. Three months after use of the Medtronic Guardian sensor she developed ACD, patch testing was performed and was positive to isobornyl acrylate. A second child, developed ACD to Dexcom G6, having used it for several years, this coincided with a change in the manufacturing process. In both cases placement of the barrier (Compeed) prevented any further ACD. This method has helped to maintain excellent diabetes control (table 1) with no adverse impact on sensor function. This method is now used routinely when ACD arises from Dexcom G6 CGMD in our service allowing on-going use of HCL system. We highlight two cases where barrier use has allowed continued quality of life and excellent diabetic control.

Table 1

	HBA1C	
Child	Range	Mean
1	50–56 mmol/mol	53
2	46–63 mmol/mol	52

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Neonatal diabetes experience from a single centre

Olcay Evliyaoglu[1], Elvan Bayramoglu[1], Hasan Karakas[1], Dilek Aydın[1], Elisa De Franco[2] & Hande Turan[1]
[1]Istanbul University-Cerrahpasa, Istanbul, Turkey; [2]University of Exeter, Exeter, UK

Background

Neonatal diabetes mellitus is a rare form of monogenic diabetes which is diagnosed in the first six months of life. Eight patients with neonatal diabetes presenting to a single centre were studied for clinical presentation,genetics and treatment outcomes.

Objective

Eight children (2 f/6m) presenting to a single centre in Turkey were studied for correlation of disease with clinical features and genetics, suitability of current treatment regimens and treatment outcomes.

Method

Genetic studies were performed on all clinically diagnosed patients. Demographic and laboratory data (HbA1C, blood glucose, liver and kidney function tests and autoimmune markers) were recorded from the files.

Results

Age at diagnosis ranged from 1 day to 1 month. Genetic mutations were identified in five of the eight children. One children had mutation in KCNJ11 gene, 4 children (3 of them from the same family) had PTFA1 mutation. Pancreatic exocrine dysfunction was observed in 5 patients, 4 of these were with mutations in the distal PTF1A enhancer and one of them wasn't detected any mutations. Seven patients were born small for gestational age to consanguineous parents. Except for the case with Dend syndrome, single insulin glargine was started firstly and added rapid acting insüline to this theraphy during follow-up. Insulin pump was inserted in 3 cases. One of patients' fathers was also homozygous for the PTF1A mutation, whilst his partner and the parents of the other patient were heterozygous carriers. In the case with DEND sydrome (delayed KCNJ11 mutation, p.Cys166Tyr (c.497G>A), was identified. This patient was born to nonconsanguineous parents with normal birth weight. The majority of neonatal diabetes patients with KCNJ11 mutations will respond to sulphonylurea treatment. Therefore Glibenclamide, an oral antidiabetic of the sulphonylurea group, was started. This treatment regimen relatively improved blood glucose levels and neurological symptoms in the short term.

Conclusion

With proper genetic analysis, basic research findings can be translated into accurate treatment decisions and good clinical outcomes in neonatal diabetes and especially, the outcomes of transition onto sulphonylurea can be improved. Although neonatal diabetes mellitus can be diagnosed clinically, genetic analysis is important since it is a guide for the treatment and for prognosis.

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P116

Abstract withdrawn

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P117

A rare case of metabolic encephalopathy complicating diabetic ketoacidosis

Claire Reynolds[1], Sami M Alanazi[1], Declan Cody[1], Susan M O'Connell[1,2], Tracey A Conlon[1] & Lisa Corley[3]
[1]Department of Diabetes and Endocrinology, Children's Health Ireland at Crumlin, Dublin, Ireland; [2]Department of Paediatrics, Royal College of Surgeons of Ireland, Dublin, Ireland [3]Department of Neonatology, Rotunda Hospital, Dublin, Ireland

A previously healthy 12 year old girl presented to the emergency department with loss of consciousness and increased work of breathing. She was unwell for 3 days prior to presentation with vomiting and lethargy. There was a 3 week history of polydipsia and weight loss. On assessment, Glasgow Coma Scale (GCS) was 7/15, pupils size 3, equal but poorly responsive. She was hypertensive BP 140/70 mmHg, HR 113 bpm, and capillary refill time 5 seconds. There was left arm decorticate posturing on exam, with no other focal neurology noted. Initial investigations revealed blood glucose 22 mmol/L, ketones 4.8 mmol/L, pH unrecordable, Na 132 mmol/L, K 4.5 mmol/L and CRP < 5 mg/L. Urine toxicology was negative. The working diagnosis was severe diabetic ketoacidosis (DKA) with clinical evidence of cerebral oedema. She was intubated and ventilated and resuscitated with 3% hypertonic saline. DKA protocol was commenced and she received IV Ceftriaxone to treat possible sepsis. CT brain reported no acute abnormality or cerebral oedema. She extubated later that day but was not moving her limbs or talking and she did not appear to recognise her parents. Following consultation with Neurology, a repeat CT brain with contrast was performed, which ruled out sagittal vein thrombosis. EEG reported generalised slowing with superimposed rhythmic fast activity with anterior predominance; findings consistent with moderate encephalopathy and the possibility of a locked-in or brain-stem syndrome. She improved clinically within 24 hours; GCS 15/15, she was alert, orientated, moving all 4 limbs, and communicating appropriately. A diagnosis of metabolic encephalopathy secondary to severe DKA was reached. She was switched to subcutaneous insulin after 48 hours on the DKA protocol. On follow up, she has no apparent cognitive or motor impairments. Metabolic encephalopathy is an extremely rare but potentially devastating complication of DKA. This is the first reported case of metabolic encephalopathy complicating DKA in the paediatric population. While our patient was critically ill, her encephalopathy was transient and reversible. The aetiology is still poorly understood. A high clinical suspicion, along with strict monitoring of fluids and electrolyte balance is necessary to ensure early detection, appropriate management and improved long-term outcome in this group.

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P118

Adaptation of local practice guidelines increases paediatric doctor confidence in prescribing multiple daily injections for newly diagnosed type 1 diabetics at discharge

Haris Shoaib, Yunus Hussain & Shahida Ahmed
Basildon & Thurrock University Hospital, Basildon, UK

Background
There exists low confidence in prescription of multiple daily injections (MDI) for newly diagnosed Type 1 Diabetes Mellitus paediatric patients among paediatric doctors at Basildon & Thurrock University Hospital (BTUH).
Aim
To improve the confidence in MDI discharge prescriptions for paediatric doctors of all grades via adaptation of local guidelines.
Methods
We designed an adaptation of existing local guidelines as posters to enhance familiarity of MDI prescription guidance and avoid prescription errors. The intervention was delivered in a single paediatric unit to doctors of all grades. Feedback was collected and the confidence of doctors in their MDI prescriptions was evaluated pre- and post-intervention. Questionnaires were distributed to all paediatric doctors within the unit assessing their confidence in MDI prescriptions with a numerical scale of 1–5, and whether they routinely referred to existing local guidelines. Existing guidelines were adapted in consultation with the local paediatric diabetic MDT, and East of England paediatric diabetes network to display MDI guidance in a more concise format, with example MDI discharge criteria. These guidelines were distributed to the paediatric MDT via email, and displayed in visible areas of the department.
Results
Of the 13 doctors surveyed, 10 provided pre- and post-intervention feedback (77%), with statistical significance calculated via unpaired *t*-tests. 90% of paediatric doctors routinely refer to local guidelines for guidance on MDI prescriptions. However, 50% felt that existing local guidelines were not easily accessible, taking into consideration time and ease when locating them. The pre-intervention mean confidence score for completing MDI prescriptions was 1.9 (S.D. 0.83), increasing to 4 (S.D. 0.63) post-intervention (95% CI 2.79–1.41, $P < 0.0001$). 90% of paediatric doctors felt that the design and display of the MDI guidelines optimised patient care.
Conclusions
Following presentation in the local audit and QI meeting, the adapted guidelines were included in the junior doctor induction programme and made available on the local intranet. Adaptation of local guidelines to include MDI prescription guidance has shown an improvement in confidence of MDI prescriptions for paediatric doctors, with the vast majority finding the intervention significant for the optimisation of patient outcomes.

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P119

A rare case of diabetes mellitus and congenital deafness in an 18 month old girl with Wolfram like syndrome

Nabeel Abdul Kareem[1], Gita Modgil[1], Sarah Bridges[1] & Toby Candler[2]
[1]Somerset NHS Foundation Trust, Taunton, UK; [2]University Hospital Bristol and Weston, Bristol, UK

Background
Wolfram Syndrome (WFS) is a rare genetic progressive neurodegenerative disorder caused by mutation in the gene encoding Wolframin, a protein located in the endoplasmic reticulum. WFS has an estimated prevalence of 1 in 770 000.The hallmark features are Diabetes Mellitus, Diabetes Insipidus, Optic Atrophy, Deafness(DIDMOAD) and neurodegeneration. Classic WFS1 is inherited in an Autosomal Recessive manner whereas the Non-classic form is Autosomal Dominant either from an affected parent or as a de novo mutation.
Case
We present a term female infant with normal antenatal history. She was confirmed to have Bilateral Sensorineural hearing loss soon after birth. Subsequent genetic testing for congenital deafness identified the infant to be heterozygous for the WFS1(c2425G > Ap.Glu809Lys) pathogenic variant indicating Wolfram like spectrum disorder(the rare non-classic form of WFS).The family were counselled that the development of any osmotic symptoms should prompt a clinical review. Now 18 months old, this Caucasian girl presented with osmotic symptoms of polyuria, polydipsia and weight loss. She was diagnosed with Diabetes Mellitus(blood glucose of 25 mmol/L).She was not in DKA (with a pH of 7.43) .Investigations from a diabetes perspective demonstrated negative autoantibodies for GAD,IA2 and Zinc Transporter confirming she had an Insulin dependent non autoimmune diabetes, characteristic of WFS. There was no pathogenic variant detected in either of the parents which points towards a *de-novo* heterozygosity. She was initially managed with a combination of rapid (Aspart) and long acting(Degludec) insulin. Due to persistent episodes of hypoglycaemia, she was switched to ultra-rapid Aspart insulin analog, adjusted to the carbohydrate content,with a very good response. Transition to Insulin pump therapy and a hybrid closed loop system is being considered as an option for optimising diabetes care.
Conclusion
There is no cure for this condition. Supportive care is provided by MDT and regular surveillance is recommended for monitoring existing and emerging manifestation along with genetic counselling for future pregnancies. The WFS clinic for the whole of UK lies in two centres in Birmingham: Children's hospital and Queen's Elizabeth Hospital for paediatric and adult patients respectively.

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Gonadal, DSD and Reproduction 2

P120

Multidisciplinary team management in an andrology service for Klinefelter Syndrome: A review of current practice

Vasiliki Alexopoulou[1], Katerina Bambang[2] & Senthil Senniappan[1]
[1]Department of Endocrinology, Alder Hey Children's Hospital NHS Trust, Liverpool, UK; [2]Department of Reproductive Medicine, Liverpool Women's NHS Foundation Trust, Liverpool, UK

Background
Klinefelter Syndrome (KS) affects approximately 1 in 500 males and presents with different phenotypes. KS affects spermatogenesis and causes infertility but can also impact neurocognitive and psychological development or affect other

systems like cardiovascular, dental, skeletal. European Academy of Andrology has published recommendations regarding holistic KS management, including the fertility aspects, from childhood until adulthood.
Objectives
This project aims to examine the current management of children and young people (CYP) with KS in a paediatric tertiary hospital with a focus on fertility.
Methods
We audited our practice against European Academy of Andrology Guidelines on KS. All the patients with KS were identified and their hospital electronic records were used to extract data retrospectively.
Results
We identified 32 patients with KS. The mean age for referral to endocrine service was 10.5 years and to the andrology service was 13.6 years. Growth and development were monitored closely in all the patients (100% had weight, height and physical examination performed regularly). Majority of cases (75%) had hormonal profile (LH, FSH, testosterone) regularly monitored and in 56% of cases AMH and inhibin B were performed as well. Vitamin D levels and bone profile were checked in 37% of patients. Fertility was discussed in 76% of the cases. Testosterone was offered to 15/32 (46%) patients and the main indication was induction of puberty. Semen analysis was offered in 9 patients who were progressing with puberty spontaneously and were not on testosterone therapy but only 7 accepted the procedure. Only 1/7 patients were eligible for cryopreservation and 6/7 were offered microTESE (mTESE). Educational problems were identified in 53% of cases, speech, and language problems in 65% and psychosocial problems in 68%. Genetic counseling was offered in 40% of cases.
Conclusion
Patients with KS have various needs including fertility support. Management in an MDT setting including endocrinologist, fertility specialist and psychologist is essential and can enhance individualized care and optimal management of the patient with KS and their family.

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P121

Characterising puberty in children and young people with Alstrom Syndrome

Ijeoma Anwunah[1], Tim Barrett[2,3] & Melanie Kershaw[1]
[1]Birmingham Women's and Children's Hospital, Birmingham, UK; [2]Birmingham Women's and Children's Hospital, Birmingham, UK; [3]University Hospital Birmingham, Birmingham, UK

Background
Alstrom syndrome (AS) is a very rare multisystem disorder secondary to mutations in the ALMS1 gene, associated with infantile cardiomyopathy, retinal dystrophy, early onset obesity, and diabetes. Whilst a previous international review, including 35 males, cited pubertal delay and hypogonadism to be common, no detailed characterisation of puberty exists. This retrospective longitudinal analysis aims to describe puberty in boys with AS.
Method
Retrospective analysis of electronic records for all AS males aged 11+ years attending the Paediatric NHSE highly specialised Alstrom service between 2006 and 2023. Data was extracted on growth, co-morbidities, pubertal examination (including testicular volumes), LH, FSH, and testosterone levels.
Results
28 male patients aged between 11 and 20 years (median 14.4) were reviewed. Of 64% (18/28) boys over 14 years, 12/18 (66%) entered puberty before 14 years. An additional 3 males, not previously examined, were confirmed to be in puberty age 15.1 to 18.95 years. 7 of 10 boys $<$ 14 years at their last review had entered puberty indicating at least 67.9% (19/28) boys with AS experience pubertal timing to be in the normal range, with 22/28 (78.6%) entering puberty during adolescence. Median age of confirmed normal puberty was 13 years ($n=19$). Delayed puberty with raised gonadotrophins was confirmed in 16.7% (3/18). Two had pubertal arrest, having entered puberty at 14.5–15.5 years. One remained pre-pubertal at 17.9 years. Hypergonadotrophic pubertal arrest occurred in 21% (6/28) during adolescence irrespective of pubertal timing. 80% of boys with AS had raised gonadotrophins, including 69% with normal puberty. Testosterone therapy commenced in adolescence for 25% (7/28), median age 15.5 years. Diabetes/impaired glucose tolerance and hypertension were common and seen in 47% and 31% respectively with normal puberty, and 33% with delayed or arrested puberty. 21% with normal puberty and 33% with delayed or arrested puberty had both diabetes and hypertension.
Discussion
Pubertal timing is normal in two-thirds of boys with AS (median age 13 years), but 4 in 5 have raised gonadotrophins, and 1 in 5 experience pubertal arrest necessitating testosterone therapy during adolescence. Hypogonadotrophic hypogonadism was uncommon. Comorbidities are high with no clear impact on puberty.

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P122

Characterisation of children and young people (CYP) presenting with differences in sex development (DSD) beyond the neonatal period: A single centre retrospective observational study

Diksha Shirodkar[1], Alaa Baioumi[1,2], Dinesh Giri[3], Toby Candler[3], Christine Burren[3], Rachel Hamblin[3], Julie Alderson[3] & Elizabeth Crowne[3]
[1]Paediatric Endocrinology and Diabetes Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]Paediatrics Department, Ain Shams University, Cairo, Egypt; [3]Paediatric Endocrinology and Diabetes Department, Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK

Introduction
DSD includes variations in the development of chromosomal, gonadal, or anatomical sex and can be subdivided into (XY DSD, XX DSD, and sex chromosomal DSD). Most presentations occur in the neonatal period with atypical genitalia or discordant phenotype and antenatal genotype, but later presentations occur raising complex diagnostic and clinical management issues.
Objective
To characterise the etiological, clinical, biochemical and management profile of CYP presenting with DSD after neonatal-period in a regional DSD-multidisciplinary team in the last 25 years.
Methods
This was a retrospective database-case note study. Inclusion:CYP patients (29 days to 18 years) diagnosed with DSD from 1/1/1998 till 30/6/2023. Data analysis involved description of the presentation features, investigations, diagnosis and timeline and psychological impact.
Results
There were a total of 333 CYP {Sex chromosome DSD ($n=134$), Congenital adrenal hyperplasia[CAH] ($n=119$) and other forms of DSD ($n=81$)} who presented with DSD in the specified time period. Thirty CYP (9%) presented with either XX or XY DSD ($n=14$ and 16 respectively) and 118(35%) patients with sex chromosome DSD (Klinefelter-syndrome $n=34$;Turner-syndrome $n=84$) beyond the neonatal period. The sex of rearing was Female:Male = 26:4. In the XX and XY DSD cohort the presenting features were pubertal disturbances (15/30), atypical genitalia (8/30-of which one adolescent presented with progressive clitoromegaly in puberty), inguinal hernias (5/30) and 2/30 were incidentally diagnosed. The mean age at the time of presentation was 6.3 years($\pm$ 4.6SDS) and the most common genetic diagnosis was non-classical congenital adrenal hyperplasia seen in 50% of CYP (15/30;one had 11-beta-hydroxylase deficiency). Other diagnoses included complete-androgen-insensitivity syndrome ($n=7$), partial gonadal dysgenesis ($n=4$),17-beta-Hydroxysteroid-dehydrogenase III deficiency ($n=3$),17-alpha-hydroxylase deficiency($n=1$) and 5-alpha-reductase-deficiency($n=1$). The diagnosis made by a combination of endocrine and genetic investigations. Psychological evaluation was provided in all patients. Most challenging was discussing the implications of the diagnosis on the established sex of rearing. Gender dysphoria was apparent two cases (both 46 XY DSD) raised as females.
Conclusion
As with neonatal DSD presentations, it is essential to have a multi-disciplinary team(MDT) involvement to navigate the diagnostic, management and psychological challenge.

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P123

Testosterone therapy in Duchenne muscular dystrophy and longitudinal bone growth with metacarpophalangeal length measurement

Cara McCauley[1,2], Jennifer Dunne[3], Iain Horrocks[3], Shuko Joseph[3] & Sze Choong Wong[1]
[1]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [2]School of Medicine, University of Glasgow, Glasgow, UK; [3]Department of Paediatric Neurology, Royal Hospital for Children, Glasgow, UK

Background
Testosterone therapy is recommended for the management of puberty in Duchenne muscular dystrophy (DMD) from 12 years, according to the 2018 international standards of care with studies demonstrating improvement in linear growth. The majority become non-ambulant during mid-to-late adolescence. Accurately measuring height in non-ambulant adolescent boys can be challenging compounded by lower limb contractures. Estimated height from segmental body part measurements often overestimates actual height.

Objectives
The aim of this study was to retrospectively evaluate the efficacy of 12 months of testosterone on bone growth in boys with DMD using metacarpophalangeal length measured on radiographs.
Methods
A single observer measured the 19 tubular bones of the hand using the digital ruler on the radiology platform. Raw bone length measurements were converted into Z-scores from published paediatric normative data. To summarise the data for each patient, mean of the Z-scores for the 19 bones was calculated, referred to as the 'composite bone length Z-score.' Descriptive data are expressed as median(IQR).
Results
Median age at baseline was 14.3 years(IQR 1.3). All boys were pre-pubertal, with a median bone age delay of 2.9 years. All were receiving daily glucocorticoid therapy. Injectable testosterone was administered to 7 boys, while 7 received topical therapy. At baseline, 8/14 boys(57%) were non-ambulant, and was 9/14(64%) at 12 months. At 12 months, 13 boys were in early puberty(G2-G3), and one boy was in late puberty(G4). At baseline, all median bone-length Z-scores were significantly lower than zero($P<0.05$). After 12 months of testosterone, all bone-length Z-scores, except for distal phalanx 5, remained significantly lower than baseline. The median composite bone-length Z-score was −2.6(IQR 1.9) at baseline, and this decreased to −3.5(IQR 2.3) at 12 months($P<0.05$). The median rate of composite bone growth increased from 0.2 mm/year prior to testosterone to 0.6 mm/year – a median increase of 238%.
Conclusion
Using the metacarpophalangeal length, bone growth rate increased by over 200% after one year of testosterone. This improvement in growth rate is insufficient to achieve complete catch-up, possibly indicating the presence of growth hormone resistance due to long-term glucocorticoid

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P124

The value of the stimulated testosterone: dihydrotestosterone ratio in 46, XY DSD due to 5alpha-reductase type 2 deficiency

Chamila Balagamage[1,2], Rebecca Igbokwe[3,2], Jan Idkowiak[1,2,4] & Zainaba Mohamed[1,2]
[1]Department of Endocrinology and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [2]Birmingham Health Partners, University of Birmingham, Birmingham, UK; [3]Department of Clinical Genetics, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [4]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

Introduction
Testosterone(T) is converted to dihydrotestosterone(DHT), the most potent androgen, by the enzyme 5alpha-reductase type 2(SRD5A2). During foetal development, the masculinisation of male external genitalia crucially depends on DHT. Pathogenic variants in SRD5A2 cause 46,XY differences in sex differentiation(DSD). Early and accurate diagnosis is paramount to facilitate gender assignment since most reared as females may profoundly virilize at puberty, often resulting in gender dysphoria. The human Chorionic Gonadotropin(hCG) stimulation test aims to assess gonadal function and a stimulated T:DHT ratio of more than 10 has been suggested to confirm SRD5A2 deficiency biochemically.
Methods
This is a retrospective case note review of patients with 46,XY DSD due to genetically confirmed SRD5A2 deficiency in our large DSD service. Specifically, we have assessed the accuracy of hCG-stimulated T:DHT ratios in relation to the degree of genital undermasculinisation.
Results
14 patients were included; seven were raised as male, six as female and one as 'fluid-gender'. Two patients raised as female (diagnosed at 11 and 13 years, respectively) developed profound virilisation and gender dysphoria at puberty. The genital phenotype varied with External Masculinization Score(EMS) between 1 to 11. Nine patients (7 at infancy, 1 at four years and 1 at puberty) underwent an hCG stimulation test. In 7 patients, elevated stimulated T:DHT ratios above 10 (median:15; range:10.7–66.5) were reported. In two patients, aged 1 month and 4 years with an EMS of 4 and 11, the stimulated T:DHT ratios were 8.3 and 4.4, respectively. Both harboured compound heterozygous missense variants in SRD5A2 [P1: p.(Gly200Lys)/p.(Gly203Ser);P2: p.(Gly196Ser)/p.(Arg246Gln)]. Urinary steroid profiling(GC/MS) detected decreased 5α-reduced cortisol metabolites, as seen in SRD5A2 deficiency. There was no association between stimulated T:DHT ratios and presenting age or EMS score.
Conclusion
The stimulated T:DHT ratio has failed to confirm the diagnosis of SRD5A2 deficiency in 2/9 cases in our cohort; urinary steroid profiling appears to be superior in establishing the diagnosis biochemically. Genetic testing panels should be performed at early stages in the diagnostic work-up to establish the aetiology of 46,XY-DSD

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P125

Audit of the investigations and treatment for adolescents with irregular menstruation/suspected Polycystic Ovarian Syndrome at The Noah's Ark Children's Hospital for Wales

Katrin Aneva[1], Professor Aled Rees[2] & Dr Georgina Williams[3]
[1]Cardiff University Medical School, Cardiff, UK; [2]Department of Endocrinology, University Hospital of Wales, Cardiff, UK; [3]Department of Paediatric Endocrinology, Noah's Ark Children's for Wales, University Hospital, Cardiff, UK

Objective
Diagnostic uncertainty arises for paediatric patients when establishing a diagnosis of polycystic ovarian syndrome (PCOS) due to concurrent pubertal changes. Management decisions can also therefore be challenging. The investigations and management of patients referred to the Paediatric Endocrinology Service was audited against international guidelines.
Methods
Retrospective audit of patients referred with suspected PCOS to the Paediatric Endocrine Service in Cardiff from 2018 to 2022.
Results
26 patients were identified, median age 14.5 years, referred with symptoms suggestive of PCOS. Table 1 shows the initial investigations. Total testosterone was raised in 79%, 63% had an LH:FSH ratio greater than 1 and 56% had low SHBG levels. Pelvic ultrasounds were performed in 74% of patients, 67% of those who did not meet diagnostic criteria for PCOS had ultrasound findings consistent with PCOS, indicating the lack of specificity. 73% of patients had an elevated BMI, lifestyle advice or a referral to dietetics was made for 65% and 62% discussed or received the combined contraceptive pill.
Conclusions
Care should be taken to avoid both the under and over-investigation for PCOS during the period of physiological pubertal changes. There is an excessive reliance on pelvic ultrasounds to investigate PCOS in this age group. Early detection and regular screening for co-morbidities, such as cardiovascular disease and type 2 diabetes can aid the prevention of complications. Transitioning adolescents with PCOS to adult services facilitates long-term management. Guideline recommendations for investigations: (*) recommended, (−) not recommended.
Table 1 Frequency of investigations for suspected PCOS in primary and secondary care among adolescents

Investigation	Primary care investigation frequency (%)	Secondary care investigation frequency (%)	Overall investigation frequency (%)
FSH & LH (*)	50.0	57.7	96.3
Total Testosterone (*)	65.4	57.7	92.6
Androstenedione (−)	0	38.5	40.7
Dehydroepiandrosterone Sulphate (DHEAS) (−)	0	38.5	40.7
Prolactin (*)	61.5	15.4	66.7
Thyroid function Tests (TFTs) (*)	69.2	38.5	88.8
Oestradiol	30.8	42.3	70.4
Pelvic ultrasound (−)	15.4	38.4	74.1
Sex hormone binding globulin (SHBG)	42.3	23.0	63.0
Random/Fasting glucose or HbA1c	26.9	30.8	55.6
Fasting Lipid profile (*)	7.7	11.5	18.5
Free androgen index (*)	7.7	3.8	7.4
Anti-Mullerian Hormone (AMH) (−)	0	3.8	3.7
17-Hydroxyprogesterone (17-OHP) (*)	0	23.1	22.2
Urinary steroid profile	0	11.5	11.1

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P126

A case of 46, XY differences of sex development (DSD) due to FKBP4 deficiency: A novel candidate of androgen insensitivity syndrome?

Chamila Balagamage[1,2], Rebecca Igbokwe[3,2], Hannah Robinson[4], Liam McCarthy[5], Harish Chandran[5], Caroline Godber[6], Zainaba Mohamed[1,2] & Jan Idkowiak[1,2,7]
[1]Department of Endocrinology and Diabetes, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [2]Birmingham Health Partners, University of Birmingham, Birmingham, UK; [3]Department of Clinical Genetics, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [4]Exeter Genomics Laboratory, Royal Devon University Healthcare NHS Foundation Trust, Exeter, UK; [5]Department of Paediatric Urology, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [6]Department of Clinical Psychology, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [7]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

Introduction
FKBP prolyl isomerase 4, encoded by the gene FKBP4, is a member of the FK506-binding protein family and is presumed to be a regulator of the androgen receptor (AR) pathway. Mutations in FKBP4 have been proposed to cause Androgen Insensitivity Syndrome (AIS), with only one case reported in the literature so far.
Aim
To report the clinical, biochemical and genetic findings in an infant with 46, XY DSD a homozygous variant in the FKBP4 gene.
Case report
The baby (46,XY) was born prematurely at 27 weeks of gestation and noted to have severe undermasculinisation (minimal phallus with 0.5 cm in length, urethral meatus at the base, unfused labioscrotal folds, and right-side undescended testis with left testis in the groin; external masculinisation score = 1). There were no obvious dysmorphic features. Endocrine work for DSD (at term) revealed a baseline testosterone (T) level of 0.5 nmol/l, raising to 15.5 nmol/l post hCG stimulation. Ultrasound imaging detected both testes at the inguinal ring and no evidence of Mullerian structures. A next-generation multi-gene DSD sequencing panel did not detect any variants associated with DSD, including the AR gene. In the absence of a molecular diagnosis of CAIS and intense consultation with the parents who have traditional, non-binary values, the gender was assigned as male. However, subsequent whole-exome sequencing revealed a homozygous splice variant in FKBP4 (c.106-2A>G). We did not observe any masculinisation of the external genitalia following three monthly injections of 25 mg testosterone IM. At 12 months of age, the child underwent a Ross procedure for severe aortic and mitral regurgitation. There is a significant global developmental delay with delayed myelination on MRI brain imaging.
Summary and conclusion
We report a case with 46,XY DSD with a splice variant in FKBP4. The case highlights management challenges in 46,XY DSD when there is discordance between a clinical phenotype of AIS in the absence of an established molecular cause. Given the known role of FKB4 in the regulation of androgen receptor signalling, FKBP4 deficiency might extend the molecular spectrum of AIS, but functional studies and data on long-term outcomes are needed.

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P127

Complexities of gender assignment in 17β-hydroxysteroid dehydrogenase type 3 deficiency

Maira Riaz, Mehrunnisa Yasir, Heeranand Rathor & Mohsina Ibrahim
National Institute of Child Health, Karachi, Pakistan

17-beta hydroxysteroid dehydrogenase 3 deficiency is a condition that affects male sexual development. People with this condition are genetically male, with gonads (testes) intact. Their bodies, however, do not produce enough testosterone. Testosterone has a critical role in male sexual development, and a shortage of this hormone disrupts the formation of the male phenotype of external genitalia before birth.
Case report
12 years old, reared as girl, weighing 36 kg, follow up case of DSD. The patient first consulted medical advice at the age of 6 months for having right inguinal hernia. On examination female genitalia with right inguinal swelling which was tender. There Endocrine workup revealed bilateral Undescended testes (Rt measuring 1×0.4 cm and Lt 0.8×0.3 cm) and there was no evidence of uterus and ovaries. Her and chromosomal analysis showed 46 XY. The testosterone response to HCG was not conclusive (pre HCG <20, post HCG testosterone 20. After multiple sessions of counselling and discussion regarding gender of rearing the parents decided to continue her as a girl, so the testes removed surgically at the age of 1-year. Her genetic workup was done and came out to be homozygous positive for HSD17B3 variant gene which is responsible for 17 beta hydroxysteroid dehydrogenase deficiency. Her recent gonadotropins are very high (FSH is 157 mIU/mL and LH is 52.1 mIU/mL) and estrogen is low. Currently the girl is doing well on exogenous estrogen therapy. Her younger sibling having the similar problem is on list for genetic workup.
Conclusion
Although existing data are limited, early orchiectomy is likely to result in retention of female gender identity, avoiding the complications related to virilization in adolescence. As such, it is important to pursue a definitive diagnosis to guide clinical decisions, and to have the support and long term follow up with an inter-disciplinary disorders of sex development team.

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P128

Challenging clinical scenario: Germ cell tumor masquerading as peripheral precocious puberty in a one-year-old boy from Pakistan

VershaRani Rai, Professor Mohsina Noor Ibrahim, Maira Riaz & Roshia Parveen
Pediatric Endocrine Department, National Institute of Child Health, Karachi, Pakistan

Peripheral precocious puberty (PPP) in males is a rare condition characterized by the premature activation of the hypothalamic–pituitary–gonadal axis, resulting in the early onset of secondary sexual characteristics. We present the case of a one-year-old boy from Pakistan who exhibited PPP along with a left hip region mass.The patient's initial workup revealed remarkably elevated levels of beta-human chorionic gonadotropin (Bhcg) and serum alphafetoprotein (AFP), indicating potential malignancy. Additionally, his testosterone levels were significantly elevated, while follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels remained within normal ranges.Ultrasound examination of the left hip region unveiled an 8.1 cm×7.3 cm heterogenous mass, suggesting the possibility of an underlying pathology. Further evaluation through magnetic resonance imaging (MRI) of the lumbosacral region revealed a 9.5 cm×7.2 cm mass, supporting the presence of a tumor. Subsequent biopsy of the mass exhibited features consistent with a germ cell tumor, with the presence of Schiller–Duval bodies, a histopathological hallmark. Additionally, positive immunohistochemistry further confirmed the diagnosis.Germ cell tumors are uncommon in young children, making this case particularly intriguing. The occurrence of peripheral precocious puberty in conjunction with a germ cell tumor in a one-year-old boy poses a significant diagnostic and management challenge. Further investigations, such as genetic testing and molecular analysis, may be warranted to identify any underlying genetic abnormalities associated with this presentation.Treatment options for this case include a multidisciplinary approach involving surgical resection, chemotherapy, and, potentially, radiation therapy, depending on the tumor's characteristics and stage. Regular monitoring and follow-up are crucial to assess treatment response, monitor hormone levels, and detect potential complications. This case report highlights the importance of considering germ cell tumors in the differential diagnosis of peripheral precocious puberty, even in very young children. It underscores the significance of thorough evaluation, histopathological examination, and appropriate management strategies to optimize outcomes in such rare and challenging cases.

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P129

Kallmann syndrome: A FGFR1 mutation

Marisa Clemente, Eiman Naghmuish & Kamal Weerasinghe
Wrexham Maelor Hospital, Wrexham, UK

Introduction
Kallmann syndrome (KS) is a developmental disorder characterised by hypogonadotropic hypogonadism and anosmia. 30% of cases are related with genetic causes, with FGFR1 mutations being identified in 10%. There are more than 140 FGFR1 gene mutations identified. We present a female patient with KS due to a FGFR1 mutation, where the presenting features included primary amenorrhoea and anosmia.
Case description
A 16 year old female presented with primary amenorrhoea, anosmia and severe acne. She firstly noticed axillary hair at the age of 9 years, subsequently pubic hair

at 13 years old but this was sparse and covering a small area. Her weight was 62.4 kg (following 75th centile) and a static height of 158.2 (between 9th and 25th centiles; MPH 50thcentile). She had an uneventful antenatal and perinatal history. Family history of maternal ovarian cancer. Maternal menarche at 13 years of age. She has a 14 year old brother with anosmia showing pubertal development. Physical exam: sturdy build, Tanner III, one café aux lait spot in abdomen, otherwise unremarkable.
Investigations
Blood tests: ACTH, cortisol, thyroid profile, liver and renal function and growth factors all within reference ranges. LH 3.1 IU/L, FSH 6.6 IU/L, testosterone 1.2 nmol/L, progesterone <1 nmol/L. Renal and pelvic USS: normal renal and bladder findings. No structural abnormality of uterus or adnexa. Bone age (TW 2 score 988): 14.3 years at a chronological age of 16.75 years. MRI pituitary gland: no abnormality detected. Molecular genetics: heterozygous for the pathogenic variant c.1118delT p. (Leu373A rgfsTer27) in the FGFR1 gene. This result confirms a diagnosis of hypogonadotropic hypogonadism 2 with anosmia.
Management and discussion
Started on combined pill. Menstrual spotting started after 2 months. On retinoic acid for acne as per Dermatology. Sibling is under investigation, awaiting molecular genetics to rule out KS. Hormone replacement therapies are used to stimulate the development of secondary sexual characteristics at the time of puberty, and later to induce fertility. There is currently no treatment for olfactory deficit.

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Miscellaneous / other 2

P130

Patient attendance in virtual paediatric and adolescent gynaecology clinics since the COVID-19 pandemic

Keerthana Soundararajan[1] & Charlotte Elder[1,2]
[1]University of Sheffield, Sheffield, UK; [2]Sheffield Children's NHS Foundation Trust, Sheffield, UK

Introduction
The COVID-19 pandemic accelerated the execution of the 2019 NHS Long Term Plan with rapid introduction and widescale uptake of virtual consulting. While these are associated with lower Was Not Brought (WNB) rates, we observed that patients in our Paediatric and Adolescent Gynaecology (PAG) clinics were frequently absent, with parents (usually mothers) attending alone, unlike Face-To-Face (F2F) consultations, where the patients are always present. To investigate this, we explored patient attendance in virtual PAG consultations.
Methods
Our retrospective observational study reviewed all clinic letters from a single consultant's virtual PAG consultations at a UK specialist Children's Hospital from 26/3/2020 to 1/3/2023. Demographic data, WNB rate, consultation medium (video or telephone), parent/carer attendance and patient attendance with reason for absence if applicable, were analysed using Pivot Tables.
Results
All 274 virtual consultations from the study period were analysed. Patients' age ranged from 10 to 18 years (mean: 14.5 ± 1.9yrs, median & mode: 15yrs). WNB rates were 16% for F2F consultations compared to 8% for virtual consultations ($P=0.0036$). Of the virtual consultations that took place 72.3% were conducted by telephone and 27.7% by video, with the proportion of video consultations increasing over time from 2% in 2020 to 57% in 2023. Overall, patients were absent in 30% of virtual consultations compared to 0% in F2F. Absence was higher in telephone (36%) compared to video (13%) consultations ($P=0.0001$). Whilst absence was more likely in younger patients, the phenomenon was observed at all ages studied (10–18 years). Reasons for patient absence included being at school (54%), having developmental or learning difficulties (15%) and being asleep (7%).
Discussion
Despite lower WNB rates in virtual consultations, patients were frequently absent. During adolescence, young people are transitioning to take ownership of their health. Arguably this is particularly important in a PAG clinic where hormonal contraceptives are being prescribed. Reduced attendance could affect the young person's readiness to transition, potentially increasing anxiety. Without the patient, age-appropriate conversations cannot take place and healthcare professionals are prevented from exploring potential safeguarding issues. This study emphasises the importance of ensuring adolescent patient attendance while digitalising and optimising NHS services.

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P131

Hypernetwork analysis: A novel approach for epigenome analysis, with Kabuki syndrome as an exemplar

Evgenii Martirosian[1], Sara Cuvertino[1], Terence Garner[1], Bridgious Walusimbi[1], Susan Kimber[1], Siddharth Banka[1,2] & Adam Stevens[1]
[1]The University of Manchester, Manchester, UK; [2]Manchester University NHS Foundation Trust, Manchester, UK

Background/objectives
Kabuki Syndrome 1 (KS1) is a neurodevelopmental disorder caused by loss-of-function of histone 3 lysine 4 mono-methyltransferase KMT2D. In addition, to neurodevelopmental features, some Kabuki Syndrome patients also exhibit endocrine-related phenotypes, such as hypoglycaemia. KMT2D is involved in global gene regulation, therefore, it is important to have a systems-based approach to understand pathomechanisms of KS1.
Methods
DNA methylation samples from blood were used to extract differentially methylated points (DMPs), which were used for systems analysis.
Results
In KS1 cohort ($n=22$) we identified 2002 DMPs (753 hypermethylated and 1249 hypomethylated; adjusted P-value $< 1\times10-4$), compared to Control ($n=138$). Focussing on genomic regions with >7 contiguous (in *cis*) hypermethylated or hypomethylated DMPs, we identified 17 significant differentially methylated regions (FWER <0.05, 11 hypermethylated and 6 hypomethylated) associated with organ morphogenesis and skeletal system development pathways, with 13 DMRs being novel for KS1. This approach, however, failed to extract functional relevance of $>90\%$ DMPs form our data, therefore, we performed hypernetwork analysis to identify indirect co-ordinations between DMPs. This revealed 986/2002 DMPs to be highly co-ordinated (strongly correlated but majority in *trans* and not necessarily methylated in the same direction) in KS1. These DMPs were enriched for genes associated with extracellular matrix organization, cartilage development and neuronal migration. Finally, using an iterative analysis of 1000 network simulations we detected significantly lower Shannon entropy in KS1 compared to controls ($P<1\times10-4$). This shows more ordered and less diverse co-ordination of DMPs in KS1 compared to Control. The analysis of entropy within Gene Ontology processes has shown that DNA methylation associated with Interleukin-17-mediated signalling pathway and Microtubule bundle formation is more ordered in KS1 samples compared to controls.
Conclusions
Hypernetwork approach is useful in quantifying network-level differences, and in extracting deeper mechanistic insights into the fundamental pathophysiology of genetic disorders, which might be overlooked with traditional DNA methylation analyses. This is especially important with rapid increase in patient-derived epigenome data, as this approach may have significant translational potential.

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P132

Initial accuracy and family experience evaluation of the Dexcom G7 continuous glucose monitor for hypoglycaemia due to hyperinsulinism

Chris Worth[1,2], Sarah Worthington[1], Sumera Ahmad[1], Elaine O'Shea[1], Maria Salomon-Estebanez[1] & Indraneel Banerjee[1,2]
[1]Royal Manchester Children's Hospital, Manchester, UK; [2]University of Manchester, Manchester, UK

Background
For children with congenital hyperinsulinism (HI), detection and avoidance of hypoglycaemia is the cornerstone of clinical management and poses significant demands on families. Standard of care remains intermittent fingerprick monitoring but the lack of predictive information has resulted in continuous glucose monitoring (CGM) increasing in popularity. Accuracy is suboptimal in this group and family feedback identifies various barriers to use. We aimed to undertake the first evaluation of accuracy and patient experience in the recently released Dexcom G7.
Methods
Ten patients using the Dexcom G6 for the previous two months were switched to the Dexcom G7 for a further two months. Using a ContourNextOne glucometer, patients performed at least four fingerprick checks per day and when CGM reported hypoglycaemia <3.5 mmol/L. Families completed a questionnaire regarding the G6 and G7 devices.
Results
Clinical accuracy of the G7 device was better than the G6, with more of the 2036 paired values in Zone A (no risk) on the Hypoglycaemia Error Grid (93% vs 86%, $P<0.001$ on chi square) and a higher mean hypoglycaemia detection rate (63% vs

37%, $P=0.02$ on paired t-test). When asked which was more accurate, 62.5% reported the G7 and 25% the G6. The G7 trended towards a lower mean absolute relative difference but was non-significant (21% vs 26%, $P=0.2$ on paired t-test). Families reported the G7 receiver was an improvement over the G6 with better battery life and smaller size. G7 sensor insertion was reported as less painful than that of the G6 but not as simple to perform. Almost all families (75%) reported that the G7 sensors were more likely to fail and not last the full 10 days.
Conclusion
In our initial evaluation study of the new generation Dexcom G7 CGM device, we identified an improvement in clinical accuracy measures although no difference in point accuracy. Families reported satisfaction with the G7 receiver and reported less pain on sensor changes. However, device utility was significantly restricted by high sensor failure rate requiring more changes and higher costs.

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P133

Patient and public involvement: Techniques used to engage with children and young people about research in congenital adrenal hyperplasia

Joseph Tonge[1], Irina Bacila[1], Nicki Barker[2], Muniba Aslam[2], Eliza Salim[3], James Walsh[4], Bob Phillips[5,6], Nils Krone[1,2] & Neil Lawrence[1,2]
[1]The University of Sheffield, Sheffield, UK; [2]Sheffield Children's Hospital, Sheffield, UK; [3]Oasis Academy Don Valley, Sheffield, UK; [4]Notre Dame High School, Sheffield, UK; [5]The University of York, York, UK; [6]Leeds Children's Hospital, Leeds, UK

Background
Incorporating the ideas and views of children and young people (CYP) with endocrine conditions from early stages in the research life cycle will increase the benefit for patients and contribute to high impact research.
Methods
We conducted two days of patient and public involvement (PPI) sessions with patients from a tertiary endocrine centre who are living with Congenital Adrenal Hypoplasia (CAH). We explored our shared understanding of the important areas of research in CAH, and the barriers CYP experience when engaging with research and aspects of their treatment. We used games and exercises to help the CYP relax dependent upon their age and preferences on the day. Funding was obtained via a PPI grant from the National Institute for Health and Social Care Research via the Sheffield Research and Design Service.
Results
Eleven CYP between seven and 22 years old took part, accompanied by carers where appropriate. Each was given a £50 shopping voucher and travel costs to compensate for a two-hour event. The most successful activities in those aged seven to ten years was a group guess-the-drawing game and construction of 'ideal hospitals' from plastic construction blocks. Those aged 13 to 16 years enjoyed engaging with a 'guess the soft drink' game, as well as a spaghetti and marshmallow construction challenge. Although engagement in this group was variable, participants responded well to a relaxed environment with minimal pressure to engage. These activities provided ice-breaking opportunities and the ability to open up discussion about CAH and the different aspects of research that are carried out in our centre. Older participants between 17 and 22 years were happy to engage in a focus group about the challenges of CAH and research into the condition, as well as discussion about ways to engage and put younger participants at ease.
Conclusions
Patient and public involvement is best conducted in children and young people with the help of games and activities to help participants to relax and engage. We present here some basic techniques and activities that have worked well to help advise on the direction of research into a rare disease.

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P134

Abstract withdrawn

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P135

Rapid-onset obesity with hypoventilation, hypothalamic, autonomic dysregulation, and neuroendocrine tumors (ROHHADNET) syndrome: A case report

UAMD de Silva, J Suntharesan, B Gunasekara, C Lakmini & N Atapattu
Lady Ridgeway Hospital for Children, Colombo, Sri Lanka

Background
ROHHAD (rapid-onset obesity with hypoventilation, hypothalamic, autonomic dys-regulation) syndrome is an uncommon disease with fatal outcome. Rapidly progressive obesity in early childhood along with altered hypothalamic and autonomic function and hypoventilation are characteristic features. Neuroendocrine tumors complicate approximately 40% of the ROHHAD cases (ROHHAD-NET). Early diagnosis of this extreme rare disease is hampered by the absence of high degree of suspicion. Here we describe a child with ROHHAD-NET syndrome who presented with rapidly progressive obesity along with uncontrolled hypertension.
Case report
Two year and a half years old baby girl presented with recent onset of increasing weight gain. Her weight has been rapidly crossing the centile over the last 6 months while hight follows the normal centile. Her condition was associated with sleepiness, lethargy, excessive sweating, tachycardia and hyperphagia. She was borne to non-consanguineous parents via normal delivery with birth weight of 3.150 kg. Her development milestone was age appropriate. On examination, weight was above the 95th centile and height rests on the 3rd centile. Neither cushinoid nor dysmorphic features were observed. She was hypertensive with blood pressure above 95th centile. Right suprarenal soft tissue lesion was observed in abdominal ultra sound scan which was confirmed by contrast enhanced CT abdomen. It revealed heterogenous solid soft tissue mass at the right adrenal area with fine calcification that suggestive of neuroblastoma or ganglioneuroma. Her condition was confirmed as ganglion neuroblastoma by histopathology after tumour resection. Subsequently, child successfully underwent chemotherapy and her follow up ultrasound scan urinary VMA and pituitary functions were normal.
Conclusion
ROHHADNET syndrome present with rapidly progressive obesity in early childhood and autonomic dysregulation. Timely diagnosis requires a high degree of suspicion for cases that present with an unexplained rapid-onset obesity. This case highlights the value of screening for neuroendocrine tumors in suspected patients of ROHHAD syndrome.

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P136

Aortic valve disease in two females with congenital hyperinsulinism due to activating GCK mutation

Fatemah Alhusaini[1], Antonia Dastamani[1], Clare Gilbert[1], Sarah Flanagan[2], Doha Alhomaidah[3] & Kate Morgan[1]
[1]Great Ormond Street Hospital, London, UK; [2]University of Exeter Medical school, Exeter, UK; [3]Farwaniya Hospital, Farwaniya, Kuwait

Introduction
Activating mutations of Glucokinase (GCK) gene are described as a rare genetic aetiology of Congenital Hyperinsulinism (CHI), which can cause variable disease severity. However, cardiac anomalies such as aortic valve disease have not been reported as a feature of this genetic form of CHI. We describe two patients diagnosed with GCK-CHI and aortic valve disease.
Case 1
A twelve-month-old female presented at the neonatal period with hypoglycaemia due to hyperinsulinism. Genetic testing showed a novel missense de novo variant in the GCK gene (c.644A>C; p.Tyr215Ser). 18F-DOPA PET/CT scan confirmed diffuse form of CHI. The infant failed to respond to diazoxide or octreotide monotherapy. Subsequently, a conservative approach was chosen and managed with combination of diazoxide (maximum dose 8 mg/kg per day) and Lanreotide (60 mg/4weekly) which has maintained her blood glucose stable while tolerating 8 hours overnight fast. Echocardiogram showed bicuspid aortic valve with moderate aortic valve stenosis (4.0 m/s, mean gradient 35 mmHg) which was surgically treated.
Case 2
A twelve-year-old female diagnosed in the neonatal period with CHI due a GCK gene missense variant (c.641A>G; p.Tyr214Cys). She was diazoxide partially responsive (maximum dose 15 mg/kg per day) and failed to respond to Sirolimus. Due to ongoing hypoglycaemic episodes surgical treatment was decided and the

patient had near-total pancreatectomy at the age of 17 months, with histopathology confirming diffuse form of CHI. Post-surgery, she had persistent hyperinsulinism which was managed with diazoxide, until 9 years of age when she developed insulin depended diabetes mellitus. She also developed pancreatic exocrine insufficiency 9 months after surgery and started pancreatic enzymes replacement treatment. Echocardiogram showed sub-aortic ridge attached to septum anteriorly and extending around towards right coronary cusp (4.4 m/s, mean gradient 48 mmHg), treated surgically with complete resection of thick circumferential subaortic fibromuscular ridge.

Conclusion

CHI due to activating GCK gene variants usually presents at the neonatal period, show variable severity and can be challenging to manage requiring combination of medications or even near total pancreatectomy. Aortic valve disease can be an additional feature as our cases illustrate, although the underlying mechanism is undefined. Thus, screening for aortic valve disease via echocardiogram should be considered for patients diagnosed with GCK-CHI.

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Obesity 2

P137

Effects of daily glucocorticoid on body composition in Duchenne muscular dystrophy: Isolating fat mass increase to establish weight management interventions

Erin Mcquillan[1,2], J Dunne[3], I Horrocks[3], R Mochrie[4], S Joseph[3], S Shepherd[1] & SC Wong[1,5]

[1]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [2]School of Medicine, University of Glasgow, Glasgow, UK; [3]Department of Paediatric Neurology, Royal Hospital for Children, Glasgow, UK; [4]Department of Pediatric Dietetics, Royal Hospital for Children, Glasgow, UK; [5]Department of Human Nutrition, University of Glasgow, Glasgow, UK

Background

Glucocorticoid (GC) therapy is the standard management for Duchenne Muscular Dystrophy (DMD), but its use is associated with significant side effects, including weight gain. Limited research exists on the impact of GC initiation on body composition in DMD, particularly regarding the timing of fat mass increase.

Objective

This study aimed to assess changes in growth parameters, namely height-SDS, weight-SDS, body mass index (BMI)-SDS, lean mass index (LMI)-SDS, and fat mass index (FMI)-SDS, following the initiation of GC therapy in individuals with DMD.

Methods

Twenty-four boys with DMD began daily GC therapy (2013–2017). Eighteen who underwent DXA scans were included in this study-assessments conducted at baseline (prior to GC initiation but no more than three months after), 1-year, 2-year, and 3-year time points. Growth parameters (height, weight, BMI) and DXA-measured body composition parameters (LMI and FMI–SDS) were compared. The data were expressed as mean (S.E.M.), and statistical significance was set at $P<0.05$.

Results

The mean age at baseline was 5.2 (0.36) years. Mean height–SDS continued to decline significantly following the initiation of GC therapy, with a notable difference between the 3-year mark and baseline (difference of means: −0.99 [95% CI: −1.89 to −0.09; $P=0.03$]). No significant mean differences were observed in weight–SDS, BMI–SDS, and LMI–SDS at any time points. However, mean FMI–SDS began to rise after 1-year of GC exposure with significant differences of FMI–SDS at 3-year of GC compared to baseline (difference of means: +0.71 [95% CI: +0.20 to 1.22; $P=0.003$]) and 1-year (difference of means: +0.85 [95% CI: 0.34 to 1.36; $P<0.0001$]). After 3 years of GC (mean age: 8.6 years), 11/18 individuals (61%) were classified as overweight, obese, or severely obese, while this was observed in 9/18 (50%) at 2-years, and 5 /18 (28%) at 1-year and baseline.

Conclusion

Significant increase in fat mass occurs early, within 1-year, following the initiation of daily GC therapy in young boys with DMD. Incorporating nutritional support as part of the clinical care for all boys with DMD soon after GC initiation is paramount. National clinical pathways for management of obesity-related metabolic complications in DMD should be developed.

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P138

Genetics of early onset obesity: Initial data from a tier 3 paediatric weight management service

Katherine Hawton[1,2], Hannah Hickingbotham[3], Amy Fitzgerald[1], Julian Hamilton-Shield[4,1] & Dinesh Giri[1,2]

[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]University of Bristol, Bristol, UK; [3]Croydon University Hospital, London, UK; [4]NIHR Biomedical Research Centre, University of Bristol, Bristol, UK

Introduction

A proportion of severe obesity is due to monogenic inheritance, however access to genetic testing is often limited which may underestimate prevalence. We report our data obtained via the Rare Obesity Advanced Diagnosis™ genetic testing program established to diagnose rare genetic causes of obesity.

Methods

49 patients (22 male) under the care of a tier 3 paediatric weight management service with early-onset (<5 years of age) severe obesity (BMI ≥99.6th centile-for-age) and hyperphagia were screened for monogenic obesity variants using a targeted gene panel, consisting of 79 obesity related genes. The panel also included the genes encoding proteins in the leptin–melanocortin pathway (*POMC, PCSK1, LEPR, NCOA1, SH2B1, MC4R, MC3R, CPE, LEP, KSR2, SIM1*) and assessment of rearrangement of the 16p11.2 chromosomal region. Variants were classified as pathogenic or potentially relevant which was subdivided into suspected pathogenic (SP), variant of unknown significance (VUS), or suspected benign (SB) utilising available evidence.

Results

Patients ranged from 1.5 to 17.5 years, mean BMI–SDS was 4.0(range 2.1–6.0) and mean reported age-of-onset of obesity was 3.3 years(range 1–9). Pathogenic variants were identified in 10.2%(5/49), SP in 10.2%(5/49), VUS in 22.4%(11/49) and SB in 10.2%(5/49) of patients and one had a deletion in 16p11.2 region. *PCSKI* p.(Asn221Asp), a variant conferring polygenic risk for obesity, was found in 12.2%(6/49) patients.

Conclusions

In our cohort, variants involving genes in the *MC4R* pathway were the most frequent, representing 8.1% of pathogenic and 14.2% of potentially relevant variants. With the emergence of targeted therapies, for example the *MC4R* agonist setmelanotide for certain *MC4R* pathway variants, genetic testing for severe obesity may facilitate a deeper understanding of aetiology and enable targeted treatment.

	Genes (frequency of Potentially Relevant Variants)			
Genes (frequency of pathogenic variants)	**Suspected Pathogenic(SP)**	**Variant of unknown significance(VUS)**	**Suspected benign(SB)**	**Gene with Polygenic risk variant (frequency)**
MC4R (2) *SIM1* (2) *RAI1* (1) **Chromosomal rearrangement** 16p11.2 deletion (1)	*SEMA3A* (2) *KIDINS220* (1) *TUB* (1) *KSR2* (1)	*PCSK1* (2) *KIDINS220* (2) *SEMA3A* (1) *KSR2* (1) *MAGEL2* (1) *RPS6KA3* (1) *PLXNA3* (1) *CREBBP* (1) *GNAS* (1)	*NCOA1* (2) *EP300* (1) *PCSK1* (1) *RAI1* (1)	*PCSKI* (12)

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P139

The prevalence of monogenic obesity in Turkish children with non-syndromic early onset obesity. A multicenter study

Ayşehan Akıncı[1], Doğa Türkkahraman[2], İbrahim Tekedereli[1], Leyla Özer[3], Bahri Evren,[4], İbrahim Sahin[1], Tarkan Kalkan[4], Yusuf Cürek[4], Emine Camtosun[1], Esra Doger[5], Aysun Bideci[5], Ayla Güven[6], Erdal Eren[7], Ozlem Sangün[8], Atilla Cayır[9], Pelin Bilir[10], Ayça Törel Ergür[11] & Oya Ercan[12]

[1]İnönü University Faculty of Medicine, Department of Pediatric Endocrinology and Diabetes, Malatya, Turkey; [2]Antalya Training and Research Hospital, Antalya, Turkey; [3]Yüksek İhtisas University Faculty of Medicine, Department of Molecular Genetics, Ankara, Turkey; [4]Antalya training and research hospital, Antalya, Turkey; [5]Gazi University Medical Faculty, Ankara, Turkey; [6]Baskent University Pediatric Endocrinology, İstanbul, Turkey; [7]Uludağ University Pediatric Endocrinology, Bursa, Turkey; [8]Baskent University Pediatric Endocrinology, Adana, Turkey; [9]Erzurum Training and Research Hospital, Erzurum, Turkey; [10]Ankara University

Pediatric Endocrinology, Ankara, Turkey; [11]Ufuk University Pediatric Endocrinology, Ankara, Turkey; [12]Istanbul Cerrahpaşa University, Istanbul, Turkey

Background
Objective: Non syndromic monogenic obesity is a rare cause of early onset severe obesity in the childhood period. This form may not be distinguishable from other forms of severe obesity without genetic analysis, particularly if patients do not exibit any physical abnormalities or developmental delay. The aim of this study was to screen 41 different obesity-related genes in children with nonsyndromic early onset severe obesity.
Patients and methods
Children with severe (body mass index-standard deviation score >3) and early onset (<7 years) obesity were screened by next-generation sequencing based, targeted DNA custom panel for 41 known-obesity-related genes and the results were confirmed by Sanger technique.
Results
Six novel variants were identified in five candidate genes in seven out of 105 children with severe obesity; two in SIM1 (p.W306C and p.Q36X), one in POMC (p.Y160H), one in PCSK1 (p.W130G fs Ter8), two in MC4R (p.D126E) and one in LEPR (p.Q4H). Additionally, two previously known variations in MC4R were identified in four patients (p.R165W in three, and p.V166I in one).
Conclusion
We identified six novel and four previously described variants in six obesity-related genes in 11 out of 105 childrens with early onset severe obesity. The prevalence of monogenic obesity was 10.4% in our cohort.

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P140

Evaluation of psychological and musculoskeletal outcomes in a tertiary weight management service at the Royal Manchester Children's Hospital

Matthew Earnshaw[1], Mars Skae[2], Rhian Hughes[2], Wing Tang[2] & Salma Alim[2]
[1]University of Manchester, Manchester, UK; [2]Manchester University NHS Foundation Trust, Manchester, UK

Background
Nearly a third of children aged 2–15 are overweight or obese (body mass index at or above 95th percentile) and children are becoming 'obese' at earlier ages and staying obese for longer. Obesity is linked to an array of medical conditions including hypertension, non-alcoholic fatty liver disease, and musculoskeletal pain and is associated with poor health-related quality of life (HRQoL) overall. Yet there is limited information on the relationship between obesity and different dimensions of HRQoL. The Complications from Excess Weight Service (CEW) aims to holistically treat complications that are associated with excess weight in children aged 2–17.
Aims
To describe and evaluate the HRQoL and mobility of young people accessing a CEW service and offer recommendations for clinical interventions and further service development.
Method
A patient survey completed by both patients and parents gathered information about HRQoL across multiple domains. Additionally, 2-minute walking test data, body mass index (BMI), patient demographics, and time spent in the CEW service were also analysed.
Results
Social functioning showed the biggest HRQoL impairment across all ages of young people surveyed (-41.77 and -41.79, $P<0.001$). A change in HRQoL was independent of an improvement in BMI ($P<0.05$). Impaired HRQoL was associated with increasing age and a higher body mass index percentile (BMI–SDS) ($P<0.05$). Parent reports showed more emotional functioning difficulties when compared to self-reports which indicated more social functioning difficulties. Weight-related stigma was universally prevalent across all the young people surveyed with name-calling (68.75%), comments about size (62.5%) and shopping for clothes (56.25%) most frequently reported. Impaired mobility had a greater association with increasing age ($r=-0.515$, $P=0.001$) and a higher BMI–SDS ($r=-0.438$, $P=0.007$).
Discussion
The evaluation highlighted that children with excess weight need focused interventions to improve social functioning, and tackle self-esteem and bullying-related concerns in addition to weight management strategies. Differences in scoring in specific areas of HRQoL between parents and young people must be factored in when addressing concerns, to ensure successful whole-family approaches in setting treatment goals. Assessments and interventions to support mobility, particularly in older children and those with higher BMI are essential.

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P141

Continuous glucose monitoring highlights the limited effect of lifestyle intervention on early glycaemic dysregulation in CYP with severe obesity

Louise Apperley & Senthil Senniappan
Alder Hey Children's Hospital, Liverpool, UK

Introduction
Childhood obesity is associated with complications, such as type 2 diabetes mellitus (T2DM). The use of continuous glucose monitoring (CGM) in diabetes mellitus is well established, but there is limited research evaluating the role of CGM in childhood obesity. The aim of this study was to investigate the use of CGM in identifying glycaemic dysregulation in children and young people (CYP) with obesity and the effect of lifestyle therapy.
Methods
32 patients were recruited onto the prospective study (PD-LOOP), with 29 completing the 3-month lifestyle intervention. Anthropometric measurements, body composition data, oral glucose tolerance test (OGTT), blinded CGM (Dexcom G6) and PedsQL 4.0 generic scale questionnaire were completed at baseline and 3-months. During the 3-months, participants and their caregivers received two weekly inputs for lifestyle modification.
Results
The mean age was 14.0 years (10.1 to 16.7) with 51.7% (15/29) being female. The mean body mass index at baseline was 44.3kg/m2 (+3.74 SDS). Over the 3-months, there was no significant change in measurements or body composition. One patient progressed to impaired glucose tolerance at 3-months. The CGM was worn for an average of 8 days and showed a mean glucose of 6.4 mmol/L at baseline and 6.6 mmol/L at 3-months. The readings showed a reduction in the time that the glucose levels spent within the normal range, despite regular input for lifestyle modification. The median time within normal range (86% at baseline and 83% at 3-months) was much less than that reported in CYP without diabetes and obesity (97%). The median time spent with glucose levels over 10 mmol/L was 1% at both time-points, which was 0% in the comparison data.
Conclusion
The study has highlighted the limitations of lifestyle intervention in improving glycaemic dysregulation in CYP with severe obesity. The pilot data shows the potential of CGM in identifying glycaemic dysregulation, despite the normal OGTT results, and the potential to use CGM in monitoring the glycaemic response to therapy in CYP without diabetes mellitus. Recognising the glucose abnormalities early is crucial in developing targeted interventions to reduce the risk of progression to T2DM.

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P142

Immune modulatory response to rituximab in ROHHAD syndrome

Katherine Hawton[1,2], Andrew Hogan[3], Julian Hamilton-Shield[4,1] & Dinesh Giri[1,2]
[1]Bristol Royal Hospital for Children, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK; [2]University of Bristol, Bristol, UK; [3]Childhood Obesity Immunology Research Group, Maynooth University, Dublin, Ireland; [4]NIHR Biomedical Research Centre (Nutrition Theme), University of Bristol, Bristol, UK

Background
Rapid-onset obesity with hypoventilation, hypothalamic dysfunction, autonomic dysregulation (ROHHAD) is a rare syndrome associated with high morbidity. An immune-inflammatory aetiology has been postulated; however, the immune characteristics and effect of immunomodulation have not been well described.
Case report
We describe the immune profile and the effect of rituximab on the immunomodulation potentially causing a clinical effect of weight loss in a patient with ROHHAD. A five-year-old female presented in respiratory arrest, rapid weight gain, central hypoventilation, central diabetes insipidus, growth hormone deficiency and hyperprolactinaemia suggestive of diagnosis of ROHHAD. With no proven treatment for ROHHAD, two courses of the monoclonal antibody rituximab (750 g/m^2) were given four weeks apart to target

any underlying immune dysregulation. A cytokine profile measuring tumour necrosis factor (TNF), interleukin-6 (IL-6), interleukin-1b (IL-1b) and interleukin-1 (IL-10) levels in response to stimulation by lipopolysaccharide (LPS) and anti-cluster of differentiation 3 (anti-CD3) with interleukin-2 (IL-2) was analysed before and after treatment. These pro-inflammatory molecules (TNF, IL-6 and IL-1b) have been implicated in the development of obesity-related metabolic dysfunction, with IL-10 being metabolically protective.
Results
An inflammatory cytokine profile (table 1), with significantly raised TNF, IL-6 and IL-1b levels and low IL-10 levels in response to stimulation by both LPS and anti-CD3/IL-2 was demonstrated pre-rituximab. A reduction in TNF of nearly a third, near halving of IL-6, two third's reduction in IL-1b and a three-fold increase in IL-10 on LPS stimulation was found six months after rituximab therapy. Significant weight loss was observed (2.13 BMI–SDS reduction) in the 12-months following rituximab therapy.
Discussion
This patient with ROHHAD has an inflammatory immune profile with elevated TNF, IL-6 and IL-1b, and low IL-10, suggestive of both myeloid and T-cell lineage involvement. We demonstrate significant improvement in the inflammatory phenotype following rituximab with potential clinical benefit. Further similar studies on the immune profile in ROHHAD is warranted.
Table 1 Cytokine profile pre- and post-treatment with rituximab (pg/mL)

	TNF		IL-6		Il-1b		IL-10	
Stimulus	Pre	Post	Pre	Post	Pre	Post	Pre	Post
LPS	2150.7	1491.6	17 522.2	9723	5300.2	2000.8	586.9	1775.4
aCD3+ IL2	1269.6	1158.1	865.1	639.5	579.7	620.9	278.3	961.2

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P143

Significantly higher prevalence of glycaemic dysregulation in CYP with severe obesity as identified using CGM despite normal OGTT
Louise Apperley, Jennifer Parkinson & Senthil Senniappan
Alder Hey Children's Hospital, Liverpool, UK

Introduction
Childhood obesity is associated with complications, such as impaired glucose tolerance and type 2 diabetes mellitus. The gold standard investigation for diagnosing glycaemic alterations is an oral glucose tolerance test (OGTT). Continuous glucose monitors (CGM) are routinely used in the management of children and young people (CYP) with type 1 diabetes mellitus. The aim of our study is to investigate whether CGM is more effective in identifying glycaemic dysregulation, compared to an OGTT in CYP with obesity.
Method
38 paediatric patients under the care of a tier-3 multidisciplinary weight management service were recruited in this prospective study. Blinded Dexcom G6 CGM devices were inserted into the upper arm to obtain free-living glucose readings on 59 occasions. On each of these, the patient had a recent normal OGTT prior to the CGM being inserted. None of the patients were on any medicines effecting glucose levels.
Results
The mean age of the patients was 14.3 years (range: 10.1–16.7) with 52.6% (20/38) being female. The mean weight was 113.1 kg (+21.9 s.d.), mean BMI was 40.8 kg/m^2 (+7.7 s.d.) and average BMI SDS was +3.6 (+0.5 s.d.). The CGM devices were worn for an average of 8.1 days (range: 3–10) and the mean glucose over this duration was 6.5 mmol (+1.0 s.d.). The coefficient of variation was normal (16.9%; NR <36%). The median percentage time that the glucose levels were within range (3.9–7.8 mmol/L) was 86% (IQR 76–93). The median percentage glucose levels over 7.8 mmol/L were 12% (IQR 3–23) and over 10 mmol/L were 1% (IQR 0–1.7).
Conclusion
The results have shown that the percentage time in range for CYP with obesity (86%) is lower than that seen in healthy participants with no evidence of diabetes mellitus (95%), highlighting for the first time, the prevalence of glycaemic dysregulation in CYP with severe obesity which are missed by routine testing using OGTT. In addition, 1% of glucose readings were higher than 10 mmol/L, raising significant concerns about metabolic health and long-term complications. The study highlights the potential use of CGM devices in the early identification of glycaemic dysregulation, enabling targeted interventions by healthcare professionals to prevent long-term complications.

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P144

The impact of socio-economic deprivation on the Complications from Excess weight; Insights from a Tier 3 weight management service
Ellie Clarke, Louise Apperley & Senthil Senniappan
Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Introduction
Socio-economic factors have a huge impact on children and young people's (CYP) overall health status. The rates of childhood overweight and obesity continue to rise and the CYP from areas with higher social deprivation are adversely affected with higher rates of obesity. We report the link between socio-economic deprivation and complications from excess weight (CEW) in the CYP being managed in a tier 3 multi-disciplinary (MDT) weight management service.
Objectives
To evaluate the relationship between level of deprivation and CEW in CYP.
Methods
Retrospective data from 101 patients (53 Females) being managed as part of the MDT service were analysed. Demographic data including Index of Multiple Deprivation Decile (IMDD), age, gender, BMI, BMI standard deviation score, medical diagnoses, and CEW were included in the analysis. The IMDD was checked using the online Postcode Lookup Tool (Ministry of Housing, Communities and Local Government, n.d) for each patient's postcode ($N=101$) and allocated into IMD Deciles 1 – 10.
Results
The mean age of the CYP was 14.1 years. 54 different postcodes were identified throughout the catchment area of the service. 52.9% of the patients fell within the most deprived 10% of the lower layer super output areas (LSOAs) nationally. 2/3 of the patients live in IMDD 1–3. 70% of patients from IMDD 1 and 50% of patients living in IMDD 2 experience two or more weight related complications. All patients with type 2 diabetes mellitus (T2DM) live in the lower IMDD (level 1–4) and 50% of them live in IMDD 1.
Conclusions
Majority of patients in our cohort live in the most deprived areas suggesting a strong link between socio-economic deprivation and the prevalence of severe obesity. In addition, CYP living in the most deprived areas tend to suffer from significantly higher number of CEW including T2DM. This poses unique challenges in the management of the patients as cost of living and poverty could be potential barriers in achieving the healthy weight status. Further research to investigate the impact of poverty and deprivation on the outcomes of weight management services would be crucial in identifying targeted strategies.

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Pituitary and Growth 2

P145

Pathways linking early growth to cardiometabolic disease risk development: Novel insights from the Manchester BabyGRO Study
Chantel Lui[1], Terence Garner[1], Adam Stevens[1], Lucy Higgins[1,2], Peter Clayton[1,2], Edward Johnstone[1,2] & Reena Perchard[1,2]
[1]University of Manchester, Manchester, UK. [2]Manchester University NHS Foundation Trust, Manchester, UK

Background
Using small for gestational age (SGA) as a marker for fetal growth restriction (FGR), studies link an adverse intrauterine environment to cardiometabolic risk markers in childhood. Focusing on 3–6 year old children, where the majority were born following pregnancies at greater risk of suboptimal fetal growth (SFG) but only a minority were born SGA, cardiometabolic risk markers were measured and blood samples collected for metabolomic analysis. Nuclear magnetic resonance (NMR) data previously implicated the arginine–nitric oxide pathway, alongside higher childhood systolic blood pressure (SBP). Liquid chromatography mass spectroscopy (LCMS), a more sensitive technique, has now been applied to these specimens.
Aims
1) Determine whether differences exist in the LCMS metabolome of this cohort. 2) Use a supervised approach based on quartiles of weight trajectory to establish differentially expressed metabolites (DEMs) between groups.
Methods
Fetal and childhood growth trajectories were divided into quartiles, and cardiometabolic differences established (BSPED 2022, OC 6.2). These included SBP, HDL (both $P<0.05$) and serum insulin ($P=0.08$). K means clustering, a machine learning approach, was used to establish whether underlying differences in the LCMS metabolome exist. Cardiometabolic differences and DEMs were examined between clusters. As a supervised approach, DEMs were identified between weight trajectory quartiles and used to examine underlying metabolic pathways using specialist software, Metaboanalyst.

Results
Underlying differences in the LCMS metabolome separated participants into two groups. These differed in sum of skinfold thicknesses ($P=0.03$) and brachial augmentation index ($P=0.04$), a measure of arterial stiffness. Although 130 pathways were identified, none were significant after multiple testing correction. Supervised analyses identified pathways supporting previous findings (nitrogen metabolism, $P=0.01$, arginine/proline metabolism, $P=0.04$), as well as those relating to HDL/LDL-cholesterol (vitamin B3, $P=0.04$) and insulin resistance (carnitine shuttle, $P=0.04$).
Conclusions
Differences in the underlying metabolome exist, relating to cardiometabolic risk markers in childhood. Supervised analysis of the LCMS metabolome supported involvement of the arginine–nitric oxide pathway in relation to SBP, and revealed others involved in lipid and glucose metabolism. Integration with gene expression (transcriptome) markers within this cohort could reveal early-life markers of raised cholesterol and insulin resistance.

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P146

Predictive value of a basal LH instead of an LHRH test in assessing pubertal suppression in children on GnRH agonist therapy

Habab Easa & Taffy Makaya
Oxford Children's Hospital, Oxford, UK

Background
Historically, a second LHRH stimulation test has been the gold standard test for the evaluation of biochemical evidence of pubertal suppression in patients with central precocious puberty (CPP) following commencement of GnRH analogue therapy. However, this test is time-consuming, costly, and uncomfortable for patients.
Aims/objective
To analyse the validity of the basal LH level as a predictor to the peak LH value.
Method
We reviewed 10-years' worth of data (01/012013–31/12/2022, inclusive) as part of a service evaluation. Patients were identified from the test-results database. Electronic patient notes and biochemistry results were reviewed. Inclusion criteria included patients diagnosed with CPP based on an LH value >5 IU/L on the LHRH stimulation test, and subsequently commenced on GnRH agonist therapy. Data analysis was performed for the correlation between the basal and peak LH in the second LHRH test after commencing therapy, using a grid for evaluating a clinical test. Basal LH of ≤ 0.5 IU/L and peak LH value of ≤ 1 IU/L were considered as biochemical indicators of adequate pubertal suppression.
Results
41 patients fulfilled the criteria for CPP (85% female, $n=35$). The median age of presentation was 6.7 years in girls, and 7 years in boys. 51% of the cohort were identified as white/white British ($n=21$). In 87% of the cohort, there was no family history of precocious puberty ($n=34$). Breast enlargement (Tanner 2) was the main presenting symptoms in girls, compared to pubic hair and a testicular volume of 4–6 mLs in boys. Statistical analysis showed that a baseline LH of ≤ 0.5 IU has a 87.5% positive predictive value for a peak LH ≤ 1 IU/L on the repeat LHRH test, which indicates adequate puberty suppression. Also, a baseline LH ≤ 0.5 IU/L had a 100% sensitivity and 85% specificity for an adequate puberty suppression.
Discussion/conclusion
Basal LH serum sample of ≤ 0.5 IU/L, is a reliable indicator for puberty suppression in patients on GnRH analogue treatment for CPP, with good sensitivity and specificity. This will reduce the number of blood draws compared to the LHRH test. However, larger data need to be reviewed.

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P147

Testing a screening algorithm for the identification of growth-disorders for use in UK children

Joanna Orr[1], Thilipan Thaventhiran[2], Joseph Freer[1], Robert Walton[1], Joan K Morris[3], Leo Dunkel[1], Andrew J. Prendergast[1] & Helen L. Storr[1]
[1]Queen Mary University of London, London, UK; [2]Kings College London, London, UK; [3]St George's University of London, London, UK

Background
Screening algorithms for the identification of growth-disorders are routinely used in several countries. In the UK, the use of the Coventry consensus for the referral of children with suspected growth-disorders performs poorly compared to more sophisticated screening mechanisms used elsewhere. We aimed to test an algorithm developed to screen for growth-disorders in 2- to 8-year-old UK children.
Methods
The algorithm was tested using heights at referral for 153 children with growth hormone deficiency (GHD), Turner Syndrome (TS), small-for-gestational age with no catch-up (SGA), Noonan Syndrome, SHOX deficiency and hypopituitarism attending a London paediatric growth clinic. Randomly selected heights between the ages of 2 and 8 years old from 8603 children participating in the Born in Bradford (BiB) study were taken as the reference population. BiB children with known growth-affecting conditions were excluded. Standardized height-for-age (HSDS) and the child's distance to their mid-parental height (DMPSDS) were derived. The total sample available for DMPSDS analyses was smaller due to missing parental heights. Cut-off values for HSDS and DMPSDS were selected to identify around 1.5% of children for referral, and the sensitivity and specificity to identify children with growth-disorders were obtained.
Results
Both HSDS ($n=8756$) and DMPSDS ($n=7588$) had good diagnostic accuracy with cut-offs of -2.5 for HSDS and -2.1 for DMPSDS having high specificity (99% and 99%) and acceptable sensitivity (75% and 65%). Applying either cut-off selected 1.4% of BiB children and identified 81% of children with growth disorders. An analysis of children with GHD only ($n=86$) had good diagnostic accuracy for the same cut-offs with sensitivity of 72% for HSDS, and 60% for DMPSDS.
Conclusions
Results for the use of a growth-screening algorithm in a UK clinical sample are promising. However, there is a need to obtain data from children before a growth-disorder is suspected, rather than at referral, to understand the true potential of this algorithm to identify children for further investigation for growth-disorders. Although children with known health conditions were excluded from the BiB sample, it is likely some children will have subsequently developed growth-disorders. Longer follow-up would help improve estimates.

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P148

An audit of the management of childhood-onset growth hormone deficiency (CO-GHD) at completion of linear growth

Buddhi Gunasekara, Kirpal Adu-Gyamfi & Ranna El-Khairi
University College London Hospital, London, UK

Background
The main aim of growth hormone(GH) treatment during childhood is to attain optimal final height. As a young adult GH treatment is important to achieve optimal body composition (including peak bone mass), psychosocial development and to reduce metabolic and cardiovascular risks. At completion of linear growth (height velocity [HV] <2 cm/year), it is recommended that GH treatment should be discontinued, and GH status reassessed to determine the eligibility for adult GH treatment.
Objectives
To review whether young people (YP) with CO-GHD, who have completed linear growth, have been re-tested to determine eligibility for adult GH treatment, as per NICE clinical guidelines.
Method
Retrospective medical record analysis of 60 YP with CO-GHD who had completed linear growth, followed-up in an adolescent endocrinology centre between 2018 to 2023.
Results
Of 60 YP who had completed linear growth (ages 14.3 to 19.6 years), 28 had isolated growth hormone deficiency (IGHD) and 32 had multiple pituitary hormone deficiencies (MPHD). 15% ($n=9$) YP received adult GH therapy without retesting (of which 89% had MPHD); 68% ($n=41$) were retested with a GH stimulation test (IGHD $n=18$, MPHD $n=23$); 15% ($n=9$) are still awaiting a stimulation test; and one patient refused retesting and opted to stay off GH. An Insulin tolerance test (ITT) was performed in 39 YP who were retested; two YP had a glucagon test. The interval between completion of linear growth to retesting ranged from 3 to 23 months. All patients were off GH for at least 2 months before retesting. 92% ($n=38$) YP who had stimulation tests had a peak GH <3 mg/L (IGHD $n=15$, MPHD $n=23$). 2 YP had peak GH level >3 mg/L, and GH therapy stopped. One YP had peak GH >3 mg/L but received adult GH therapy due to severe symptoms. Starting adult GH dose was 0.2 mg to 1 mg.
Conclusion
The majority of YPs with CO-GHD were eligible for adult GH treatment after retesting, including all patients with MPHD. Practice was variable regarding

time between reaching final height and retesting, and also the starting adult GH dose.

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P149

Standard clinical diagnostic criteria for Silver–Russell Syndrome frequently overlooks monogenic causes

Helena Palau[1], Uttara Kurup[1], Miho Ishida[1], Avinaash V Maharaj[1], Justin H. Davies[2,3] & Helen L. Storr[1]
[1]Centre for Endocrinology, William Harvey Research Institute (WHRI), Charterhouse Square, Barts and the London School of Medicine, London, UK; [2]Paediatric Endocrinology, University Hospital Southampton NHS Foundation Trust, Southampton, UK; [3]Faculty of Medicine, University of Southampton, Southampton, UK

Background
A diagnosis Silver–Russell Syndrome (SRS) is important for early institution of appropriate management, access to therapy and reduces the burden of diagnostic uncertainty. SRS is molecularly heterogeneous and 11p15 LOM/upd(7)mat account for ∼60% cases. Monogenic causes include variants in HMGA2, CDKN1C, IGF-2, PLAG1 and contribute to 5% cases. Clinical SRS diagnosis requires the fulfilment of ≥4/6 Netchine–Harbison Clinical Scoring System (NH-CSS) criteria whereas a score of 3/6 warrants (epi)genetic investigations. Although the NH-CSS is useful for identifying commoner molecular causes of SRS, its use in identifying monogenic SRS causes is unclear. Phenotypic features of monogenic causes of SRS are not well described.
Methods
An extensive literature search identified clinical cases/details for: HMGA2 ($n=17$), CDKN1C ($n=18$), IGF-2 ($n=23$), and PLAG1 ($n=10$). We assessed whether NH-CSS criteria highlighted these monogenic SRS causes and the phenotypic features.
Results
NH-CSS for HMGA2: 12% scored <3/6, 23% 3/6 and 65% ≥4/6. CDKN1C: 11% 3/6, 78% ≥4/6, 11% could not be calculated. IGF-2: 4% <3/6, 9% 3/6 and 87% ≥4/6. PLAG1: 10% <3/6, 50% 3/6 and 40% ≥4/6. Relative macrocephaly (head circumference (HC) at birth ≥1.5SDS above birth weight and/or length SDS) was not observed in 71% HMGA2 (29% had microcephaly, HC ≤ −2SDS), 17% CDKN1C, 9% IGF-2 and 70% PLAG1 (30% microcephaly). Body asymmetry was infrequent: 6% HMGA2, 11% CDKN1C, 30% IGF-2. Other clinical features included: HMGA2 12% gastroesophageal reflux and 12% delayed bone age. CDKN1C: 6% motor and/or speech delay, 6% learning disabilities, 6% challenging behaviour/inattention, 11% diabetes, 11% adrenal insufficiency, 6% asthma. IGF-2: 65% speech/motor/developmental delay, 9% learning disabilities, 39% cardiac abnormalities, 30% cleft palate, 35% male genital abnormalities, 17% placental hypoplasia. PLAG1: 40% speech/motor/developmental delay, 20% gastrointestinal manifestations.
Conclusions
NH-CSS is poor at identifying monogenic SRS causes, missing 12% HMGA2, 4% IGF-2 and 10% PLAG1 cases. The presence of associated clinical features, including microcephaly and learning difficulties, should not preclude clinicians from investigating for rarer causes of SRS.

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P150

2 cases of congenital hypopituitarism due to pituitary stalk interruption syndrome (PSIS) diagnosed in the early infantile period

Chidambaram Sethuraman, Kaushik Banerjee & Maitrayee Kumarasamy
Barking, Havering and Redbridge University Hospitals NHS Trust, Romford, London, UK

Introduction
PSIS is a rare congenital abnormality characterised by a triad of thin or interrupted pituitary stalk, small or absent anterior pituitary, and an absent or ectopic posterior pituitary gland. Incidence is around 0.5/100 000 births. Clinical presentation varies according to age. We herein describe two cases of PSIS diagnosed in the early infantile period.
Case 1
A term female neonate born by emergency section with a birth weight of 2.8 kg was admitted to the neonatal unit at 4 hours of life with floppiness and up rolling of eyes. At admission she was hypoglycaemic, hypotensive, and hypothermic. She was initially treated as suspected sepsis. Blood sugars stabilised by day 7, however the baby required incubator support till day 24 of life. Endocrine investigations showed multiple anterior pituitary hormone deficiencies (low TSH, FT4, cortisol, IGF-1, IGFBP-3 and undetectable gonadotropins. MRI showed typical features of PSIS. Her genetic analysis showed LHX3 gene mutation. She is currently 7.5 years old receiving thyroxine, hydrocortisone and GH replacement and growing at a rate of 5.9 cm/year with height on 82nd centile. She also has right sided Auditory neuropathy spectrum disorder.
Case 2
An 8-week-old male infant presented to the ED with cough, difficulty in breathing and reduced oral intake. He was born at term and the neonatal course was uneventful. He was hypothermic, jaundiced, and lethargic on arrival. He was SARS CoV-2 positive, pancytopenic with deranged clotting function on the initial investigations. Hypoglycaemia evolved on rewarming, and he required 6 glucose boluses and a maximum GIR of 8.4 mg/kg per min and IV hydrocortisone. He required bair hugger support intermittently to maintain his temperature in the first week of his presentation. His endocrine investigations confirmed multiple anterior pituitary hormone deficiency (low FT4, ACTH, Cortisol, FSH, LH, IGF-1). MRI brain showed features of PSIS. He improved clinically after starting thyroxine and hydrocortisone. He is currently 4 months old, under follow-up
Conclusion
PSIS diagnosed in the neonatal period has a particularly severe hormonal and radiological phenotype which is true from both of our cases. Early diagnosis and timely treatment can prevent long-term effects on growth and development.

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P151

Evaluation of etiology and clinical feature of precocious puberty among children presenting in a pediatric endocrinology department in a tertiary care hospital

Versha Rani RAI, Roshia Parveen, Prof Mohsina Noor Ibrahim & Maira Riaz
Pediatric Endocrine Department, National Institute of Child Health, Karachi, Pakistan

Background
Precocious puberty is thought to occur in 1 in 5000–10 000 people. Precocious puberty is a neglected topic in Pakistan, and little research has been done so far to examine its aetiology in our population, despite its importance and relative prevalence. Objective: To find the frequency of precocious puberty in children and to compare the clinical and laboratory parameters of central and peripheral precocious puberty.
Methods
This cross-sectional study was carried out in Karachi's National Institute of Child Health's paediatric endocrinology division between December 2016 and 2021. All patients with precocious puberty will be taken from files through non-probability convenience sampling method. Data was analyzed on SPSS version 22.0
Results
Total 65 patients were included. The mean age was 6 + 3.35years. Precocious puberty was classified as peripheral precocious puberty in 38 (58.4%), central precocious puberty in 20 (30.76%), premature thelarche in 5(7.69%) and premature pubarche in 2 (3.07%). In the peripheral precocious puberty group, CAH was found in 22(78.5%), out of which 2 patients were of rare mutation of CAH presenting with peripheral precocious puberty (DAX mutation and 11 B hydroxylase mutation,adenocarcinoma was observed in 2(7.14%) followed by Mu-cane–Albright syndrome was in 4(14.28%) and van wykgrumbach syndrome in 10 patients. Central precocious puberty was found in 20 patients hypothalamicharmartoma in 4(20%), craniopharyngioma 3(15%), hypothalamic astrocytoma 1(5.0%), genetically proven neurofibromatosis in 1(5.0%) patient and hydrocephalus 1(5.0%) and in 10(50%) patients no cause was found. All the parameters were significantly comparable with P-value < 0.05.
Conclusion
Peripheral precocious puberty was more common than central precocious puberty in this study. Etiology in majority of cases with peripheral precocious puberty was CAH and idiopathic in central precocious puberty. Central precocious puberty children showed higher height SDS, weight SDS, FSH, LH than those with peripheral precocious puberty.
Keywords: Central Precocious Puberty, Girls, Peripheral, Idiop

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P152

An unusual presentation of a giant prolactinoma

Martha McKenna & Emmeline Heffernan
Royal Belfast Hospital for Sick Children, Belfast, UK

Introduction
We report a patient with a giant prolactinoma due to Multiple Endocrine Neoplasia type 1 (MEN1) with consequential growth hormone deficiency and central hypothyroidism.
Case report
A 12-year-old girl attended the genetic clinic, as her father had MEN-1 mutation. On questioning, she reported severe headaches, increasing in frequency over several months, with fatigue and hair loss. She had breast development for over 2 years, but no menstrual periods. On examination she was on the 98th centile for weight, 50th centile for height. She had no visual impairment. Bloods showed a significantly elevated prolactin of greater than 69 000 with a mono prolactin of greater than 59 000 and MEN-1 mutation was detected. Her MRI showed a large anterior pituitary lesion in keeping with a giant prolactinoma. She was commenced on cabergoline, and prolactin levels improved. Subsequent testing demonstrated pubertal arrest, growth hormone deficiency (peak growth hormone of 2.3 ng/mL) and central hypothyroidism (thyroxine 10.7 pmol/L, TSH–1.34 mIU/L). She was commenced on growth hormone and levothyroxine with a good response. Follow up imaging has shown a reduction in size of the prolactinoma.
Discussion
MEN1 is a rare, autosomal dominant disease which most commonly presents with primary hyperparathyroidism. Only 10% of MEN1 patients present with pituitary tumours, usually prolactinomas, but this is rare in children. MEN1 is diagnosed if an individual has one MEN1 related tumour and a first degree relative with MEN1 mutation or two MEN1-associated tumours. The presentation of pituitary tumours is often varied with non-specific symptoms. They may present with signs of raised intracranial pressure, visual disturbance, symptoms of hypopituitarism (hypoadrenalism, hypogonadism and hypothyroidism) or symptoms of hormone excess (hyperprolactinaemia, Cushing's disease, gigantism). This case demonstrates a rare presentation of MEN1 with multiple complications. It also highlights the difficulties in diagnosis, as she was assessed due to her family history, despite having multiple symptoms.

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Thyroid 2

P153

Four siblings with congenital hypothyroidism-really?

Shilpa Shah[1], Noina Abid[2], Milad Darrat[1], Nadia Schoenmakers[3], David Halsall[3] & Una Bradley[1]
[1]Southern Health and Social Care Trust, Craigavon, UK; [2]Belfast Health and Social Care Trust, Belfast, UK; [3]Univeristy of Cambridge, Cambridge, UK

Introduction
Congenital hypothyroidism is caused by abnormal development or function of the thyroid gland. Early detection through heel prick screening and treatment prevents irreversible adverse neuro developmental outcome. The national screening program for congenital hypothyroidism in the UK has extremely low false positive rates. We describe 4 siblings with falsely raised TSH related to maternally transmitted macroTSH.
Case summary
4 siblings currently aged 10, 8, 3 years and 19 months presented after birth with elevated TSH on day 3–5 heel prick. These were confirmed with further blood biochemistry. All were started on Levothyroxine. Their mother, currently 39 years old has a long history of elevated TSH with normal T4 levels and clinically euthyroid, not on treatment. There is no family history of thyroid disorder. Her THRβ gene sequencing did not show any mutations. The older 3 siblings were noted to have normal thyroid ultrasound and thyroid uptake on scan and successfully discontinued thyroxine by age 30 months and remain euthyroid. When the 4th child was born simultaneous samples were sent from the mother and child for further testing. Gel filtration chromatography confirmed the presence of high molecular massTSH immunoreactivity in the samples of the mother and PEG recovery was abnormal at 21 (27–20) % in this baby. Once confirmed as the cause of falsely elevated TSH the levothyroxine was discontinued in the 4th sibling at age 1 year. Follow up bloods and development remains normal at 19 months.
Discussion
Increased immunoreactive TSH, in this case, is likely to be due to Macro-TSH, an immunoglobulin TSH complex. This can accumulate in circulation, simulating a laboratory picture of subclinical hypothyroidism. Multiple TSH assays can be affected. Macro-TSH can be detected by immuno-subtraction and dilution studies and confirmed by gel filtration chromatography. While the heel prick test is extremely sensitive and specific for congenital hypothyroidism this rare cause should be considered specially in case where consecutive siblings are tested positive.

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P154

Aetiology and the mode of presentation of congenital hypothyroidism – a 10 year single centre experience in a tertiary care centre in Sri Lanka

Dinendra Siriwardhane & Navoda Atapattu
Lady Ridgeway Hospital For Children, Colombo, Sri Lanka

Introduction
Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency which is present at birth. Thyroid hormones are crucial for early neurodevelopment. Untreated severe CH results in major neurological deficits. Therefore, if treatment is initiated early, these deficiencies can be prevented. Newborn screening for CH was first initiated in Sri Lanka in September 2010.
Methods
A retrospective cohort study was carried out in the Endocrinology clinic at the Lady Ridgeway Hospital for Children. Data was obtained using the clinic records of children who were referred as having abnormal Thyroid Functions from January 2012 to January 2022 using a researcher administered questionnaire. Sample size was calculated using Lwanga and Lemeshow equation and study sample calculated as 73.
Results
When demographic factors were analysed, out of 73 cases, 50.7% were female and 49.3% were male. 84.7% were Sinhalese, while 8.2% Muslim, 4.1% Tamil and 2.7% belonged to other ethnicities. Out of the CH babies, 8.2% were born to mothers were diagnosed with thyroid illnesses and 2.7% were born to consanguineous parents. 84.9% babies diagnosed with CH were born at term while 15.1% were born preterm. 8.2% of babies with CH had Trisomy 21. 54.2% were identified by newborn screening within 2 weeks from birth and 50.7% were started on treatment with Levothyroxine within first 2 weeks of birth. 31.5% were identified between 2 weeks to 1 month and 35.6% were started on treatment between the same time frame. Clinical features led to the diagnosis of 12.3% while 50.7% were informed via their local medical officer of health and 37.1% were informed from the hospital of birth. On neonatal screening TSH was identified as >100 mU/L in 47.9% and 27.4% had TSH between 40 and 100 mU/L. 20.5% had TSH between 20 and 40 mU/L whilst 4.1% were between 6 and 20 mU/L. Ultrasound scan findings include 31.5% with aplasia, 12.3% with hypoplasia and 4.1% with ectopic location. Thyroid gland was normal in 52.1%.
Conclusion
Our analysis helped to identify the factors linked with Congenital Hypothyroidism and also assessed the efficacy of the neonatal screening program over the past decade in Sri Lanka.

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P155

Thyroid hormones and the kidneys: Don't forget to check renal function in thyroid disease

Aisha A Aslam[1,2], Lee Martin[2], Rathi Prasad[1,2], Niki Paraskevopoulou[3], Aoife M Water[4] & Li F Chan[1,2]
[1]Centre for Endocrinology, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University, London, UK; [2]Department of Paediatric Endocrinology, The Children's Hospital at the Royal London Hospital, London, UK; [3]Department of Paediatrics, Newham University Hospital, London, UK; [4]Department of Paediatrics, University of Cork, Cork, Ireland

Background
Thyroid hormones are essential for the adequate growth and development of the kidney and also target changes in glomerular and tubular functions and electrolyte and water homeostasis. Hyperthyroidism leads to an increase in glomerular filtration rate (GFR) and renal blood flow with converse effects seen in hypothyroidism. In turn, the kidneys are responsible for the metabolism and elimination of thyroid hormones and thus renal disease can lead to significant changes in thyroid function.
Case
A 7 year old girl of South American ethnicity was referred after blood results showed thyrotoxicosis (fT4 42.1pmol/l, TSH <0.01 mU/l). She presented to her GP with a 3 week history of neck swelling. There was no history of palpitations, sweating, insomnia, loose stool or difficulty in breathing. She was described as doing fairly well in school but being overactive. She had lost 2 kg in weight. She was commenced on carbimazole 10 mg twice daily with stabilisation of her

thyroid function with respective dose reduction (ft4 21.0pmol/l, TSH < 0.01 mU/l). Due to missed appointments, whilst on treatment she developed profound hypothyroidism (fT4 3.0pmol/l, TSH >100 mU/l) accompanied with significant rise in serum creatinine to 83 umol/l (NR 30–47 umol/l), with normal urea (6.2 mmol/l), sodium (140 mmol/l) and potassium (4.2 mmol/l). Additional renal investigations were normal including renal ultrasound, urine A:CR, P:CR and microscopy. Carbimazole was ceased and both thyroid and renal function showed improvement. Carbimazole was re-started 4 months after as biochemistry showed she was hyperthyroid (fT4 28.4 pmol/l, TSH 0.01 mUL/L) with subsequently stable renal function (55 umol/l; NR 30–47 umol/l).

Discussion

We report a case of Graves' hyperthyroidism who developed profound hypothyroidism whilst on titrated carbimazole treatment due to missed appointments and subsequent impaired renal function. Given the associations of renal disease and thyroid dysfunction, the patient was investigated for possible underlying renal pathology. Prompt cessation of antithyroid drugs resulted in improvement in both thyroid and renal function. The family were further educated on the importance of close monitoring and signs of thyroid dysfunction. Patients on titrated doses of anti-thyroid medication require close monitoring of thyroid function and renal function.

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P156

Interference of heterophilic antibodies with thyroid stimulating hormone (TSH) assay leading to inappropriate treatment

UAMD de Silva, Catherine Collingwood & Senthil Senniappan
Alder Hey Children's hospital, Liverpool, UK

Introduction

The presence of heterophilic antibodies resulting in assay interference could lead to falsely high or low values in biochemical investigations. We present a case of a 5-year-old girl who had persistently high level of TSH despite Levothyroxine treatment.

History

A five-year girl was found to have an elevated plasma TSH level (24.29 mU/L) with normal Free T4 (both measured using Abbott Alinity immunoassay) while being investigated for short stature. She was clinically euthyroid and her short stature screen was normal. Thyroid peroxidase antibodies were negative, and ultrasonography of the thyroid was normal. Treatment with levothyroxine 25 μg/daily was started. Despite good compliance with the therapy being reported by her parents, plasma TSH remained persistently increased (27–47 mU/L). The dose of thyroxine was therefore gradually increased up to 75 μg/day. She remained clinically euthyroid with normal Free T4 throughout this period. As TSH did not normalize, even after 12 months of therapy, thyroxine was discontinued, and she was re-investigated as assay interference was suspected. TSH when measured by another laboratory using an alternative analytical method (Siemens Atellica) was found to be 1.82 mU/L compared with 39.76 mU/L when measured using the Abbott Alinity method. A similar result (1.28 mU/L) was obtained when TSH was measured following incubation of the plasma to remove heterophilic antibodies, confirming heterophilic antibody interference in the Abbott method. This finding excluded the possibility of thyroid pathology and led to discontinuation of the thyroxine replacement therapy.

Conclusion

Interference in immunoassays due to the presence of heterophilic antibodies can result in falsely increased or decreased analyte concentrations including TSH. Analysis of samples with suspected interference using an alternative analytical method and incubation to remove heterophilic antibodies could enhance the detection of assay interference. Caution must be exercised whilst interpreting laboratory results, especially when the clinical presentation of the patient does not match the assay results.

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Managing hypothyroidism in congenital nephrotic syndrome: A case report

Catriona McKay, Haytham Mustafa, Mairead Convery & Noina Abid
Royal Belfast Hospital for Sick Children, Belfast, UK

Introduction

Congenital nephrotic syndrome (CNS) is defined as heavy proteinuria starting within three months after birth. It affects approximately 1 to 3 per 100 000 children worldwide. The classical form is the Finnish type, caused by mutations in the nephrin gene. Approximately 50 percent of all nephrotic patients have low total thyroxine (T4) concentrations resulting from urinary losses of T4-binding globulin (TBG) and other thyroid hormone-binding proteins (transthyretin and albumin) and the T4 bound to them. We present a case of CNS (Finnish type) and the difficulties in managing the associated hypothyroidism.

The case

This infant was born at 34 weeks gestation and noted on day ten of life to be oedematous, with proteinuria and hypoalbuminaemia. She was transferred to a tertiary neonatal unit at two weeks of age and found to have abnormal thyroid function tests (TFTs). (T4 11.0 pmol/L (11.5–28.3), TSH: 20.6 mIU/L (0.72–11.0). Her Guthrie was negative for congenital hypothyroidism. An ultrasound of her thyroid showed no structural abnormalities and her MRI brain showed no abnormalities of her pituitary gland. She was commenced on levothyroxine 25 μg once a day on day 15 of life. During her admission her thyroid function proved difficult to maintain. Over a period of two months she was titrated to 100 μg of levothyroxine. Issues encountered included timing of the administration of levothyroxine and of blood sampling in relation to her albumin infusions, timing of her levothyroxine in relation to her multiple other medications, intolerance of the high volume of liquid preparation levothyroxine and the high dose of levothyroxine required to maintain her T4. Her most recent bloods, performed at a corrected gestational age of 18.5 months, demonstrate a T4 14.6 pmol/L and TSH <0.01 mIU/L on 150 μg levothyroxine, given as a crushed tablet dissolved in water (17.5 μg/kg) and she is clinically euthyroid.

Conclusion and learning

Managing hypothyroidism in CNS offers unique challenges. Children with CNS often require higher than anticipated doses of levothyroxine and thought needs to be given to the preparation used and to the timing of doses. These children should have their thyroid function checked early in their clinical course.

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Miscellaneous / other 2

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A young girl with papillary thyroid cancer, could it be DICER1 Syndrome?

Chamidri Naotunna[1], Omar Hilmi[2], Thushitha Kunanandam[3], Rosemarie Davidson[4] & M Guftar Shaikh[1]
[1]Department of Paediatric Endocrinology, Royal Hospital for Children, Glasgow, UK; [2]Department of ENT, Queen Elizabeth Hospital, Glasgow, UK; [3]Department of Paediatric ENT, Royal Hospital for Children, Glasgow, UK; [4]Department of Clinical Genetics, Queen Elizabeth Hospital, Glasgow, UK

Introduction

Thyroid cancers are the most common endocrine cancer among children, accounting for 0.5–3% of all childhood malignancies. Thyroid carcinogenesis is well established in Multiple Endocrine Neoplasia syndromes type 2, and may present with medullary thyroid cancer at young age. However, with the advancement of genetics, several other syndromes need to be considered which may lead to non-medullary thyroid cancers including DICER1 tumour predisposition syndrome, PTEN hamartoma tumour syndrome (PHTS), familial adenomatous polyposis (FAP), Carney complex and, Werner which may now be part of the differential diagnosis in a child with a thyroid mass.

Case presentation

A nine and half year old previously well girl, while accidentally palpating the neck was found to have a small, hard lump. It was not painful, no compressive symptoms, with no recent enlargement. She was clinically euthyroid and systemic inquiry was negative. A strong family history for various cancer types were noted among both maternal and paternal sides, namely ovarian, bladder, bowel cancer and Hodgkin's lymphoma, but no history of thyroid cancer. On examination there was a raised fixed non tender firm lump on right anterior neck with no lymphadenopathy. USS neck revealed 20×22 mm solid nodule in right lobe of thyroid gland with well-defined lobulated margins. Fine needle aspiration was keeping with papillary thyroid cancer (PTC). She underwent uneventful total thyroidectomy, with confirmation of PTC on histology. In view of the strong family history of different types of cancer, the possibility of DICER 1 was raised.

Discussion

DICER1 syndrome is an autosomal dominantly inherited cancer predisposing syndrome, leading to a variety of neoplastic and dysplastic lesions. Pleuropulmonary blastoma is a well-recognised, fairly specific feature detected mainly in children under 6 years of age. Other clinical presentations may include ovarian Sertoli–Leydig cell tumour (SLCT), multinodular goitre, differentiated thyroid carcinoma, pineoblastoma, and sarcomas of different sites. Due to wide phenotype and variation in presentation, the possibility of a DICER-1 mutation can often be overlooked. It is important to identify affected individuals to plan follow up and screening, and to identify other affected family members although, the overall tumour penetrance of the condition is relatively low.

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