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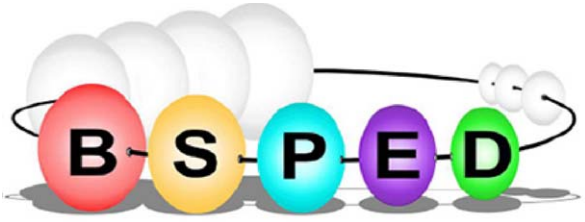

British Society for Paediatric Endocrinology and Diabetes

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CONTENTS

48th Annual Meeting of the British Society of Paediatric Endocrinology and Diabetes 2021

CME Training Day Sessions

Session 1

CME1.1

The Epidemiology of Adrenal Crises in Childhood

R. Louise Rushworth
School of Medicine, Sydney. The University of Notre Dame, Sydney, Australia

Adrenal insufficiency (AI) is a rare disorder affecting an estimated 120/million of the paediatric population. Adrenal crises (ACs) are life-threatening episodes of AI that have an incidence of approximately 5-10 /100PY, an associated mortality of up to 6%, and there is some evidence to indicate that AC incidence is increasing. AC incidence is slightly higher in primary than secondary AI, possibly due to some residual cortisol secretion in secondary AI, and some individuals appear to be at greater AC risk than others. Patient education and emergent domiciliary stress dosing are the mainstays of AC prevention but ACs continue to occur. Despite its importance, there has been little focus on research into AC epidemiology specifically in the paediatric population. The absence of a universally agreed definition of an AC for both adults and children, and the use of differing definitions between studies, make variations in AC incidence difficult to interpret with accuracy. Monitoring AC incidence on a population basis, using routinely collected datasets, assists in the evaluation of outcomes in treated AI, as small changes in the frequency of ACs may not be detectable in clinical settings. Analyses that examine incidence based on age, sex, time, and type of AI are of value, as variations within subgroups may point to possible causes or issues that may benefit from intervention. Targeted studies, such as audits of hospital admissions or clinic registers can provide more detailed information on causes of ACs in selected populations. Secondary data sources may offer further information on adherence to preventive strategies or indicate whether there are wider problems which may impact on AC prevention in a population. While no data source is perfect, and each has biases, ongoing data analysis can provide important information on AC/AI epidemiology and assist in attaining the goal of AC minimisation in AI.

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CME1.2

Abstract Unavailable

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Session 2

CME2.1

Update in the Recognition & Management of Adolescent PCOS

Lourdes Ibañez[1,2] & Francis de Zegher[3]
[1]Hospital Sant Joan de Déu, University of Barcelona, Barcelona, Spain; [2]CIBERDEM, ISCIII, Madrid, Spain; [3]University of Leuven, Leuven, Belgium

Polycystic ovary syndrome is the most common cause of hirsutism & menstrual irregularity in adolescent girls. It is often accompanied by obesity and insulin resistance and associated to lifelong co-morbidities including reduced fertility, type 2 diabetes, premenopausal cancer, depression, and pregnancy and offspring complications. There is no approved therapy for PCOS in adolescent girls. Oral contraceptives (OCs) are prescribed off-label to approximately 98% of young PCOS patients, including to those without pregnancy risk. OCs do alleviate key symptoms, such as hirsutism and menstrual irregularity by inducing the pharmacological combination of anovulatory subfertility, regular pseudo-menses, and extreme elevations of sex hormone-binding globulin, but do not revert the underlying pathophysiology, and patients remain at risk for post-treatment subfertility. New insights suggest that PCOS is, in essence, the result of a mismatch between (less) prenatal weight gain and (more) postnatal weight gain, so that there is a chronic need to store more fat than is safely feasible in subcutaneous adipose tissue. The excess fat is stored in ectopic depots, especially in the liver and viscera. The extent of such storage is partly driven by genetic and epigenetic factors, and by a low brown adipose tissue (BAT) activity, contributing to a more positive energy balance. Given that PCOS appears to be commonly driven by hepato-visceral fat excess, the focus of the treatment should be a preferential loss of hepatic fat. This reduction can be achieved with a healthy lifestyle within a multidisciplinary approach. If these measures fail, then the addition of a medication mimicking the benefits of lifestyle intervention should be considered. Pilot studies have shown that SPIOMET, a low dose combination of spironolactone (to counteract androgen and mineralocorticoid effects and to raise BAT activity), pioglitazone (to raise circulating high-molecular-weight adiponectin), and metformin (to decrease appetite and improve insulin sensitivity) normalises more than OCs the PCOS phenotype, including ovulation rates and hepato-visceral fat excess. The efficacy and safety of lifestyle intervention plus SPIOMET will be further tested in a multi-centre, double-blind, randomised Phase II clinical trial (SPIOMET4HEALTH) in adolescent girls and young adult women with PCOS and funded by the European Commission.

DOI: 10.1530/endoabs.78.CME2.1

CME2.2

Abstract Unavailable

DOI: 10.1530/endoabs.78.CME2.2

Session 3

CME3.1

Controversies in management of neonatal hypoglycaemia

Paul Thornton
Cook Children's Medical Center, Fort Worth, USA

During this session on the controversies in the management of neonatal hypoglycaemia, I will discuss why the real controversy is not the definition of hypoglycaemia but rather what we should do when we find low glucose values. I will discuss my preferred hypoglycemia guideline recommendation. In addition I will discuss the relationship between hypoglycemia and brain damage and demonstrate to the audience that hypoglycemia is not the cause of brain damage but rather energy deficiency at a cellular level in the brain is the main cause and that glucose is a surrogate marker for energy deficiency. Finally I will explain why all hypoglycemia is not equal.

DOI: 10.1530/endoabs.78.CME3.1

CME3.2

Hypothalamic obesity post cancer treatment - optimising outcomes

Robert Lustig
UCSF, San Francisco, USA

The hypothalamus integrates the neuroendocrine control of numerous hormonal systems. Energy balance is regulated by a complex neuroendocrine feedback loop, in which the ventromedial hypothalamus (VMH) responds peripheral neural and hormonal afferent signals of satiety and energy reserve (through insulin and leptin), interprets these as anorexigenic (a-MSH) or orexigenic (NPY, AgRP) signals (through the melanocortin-4 receptor), and then directs efferent autonomic signals (sympathetic or vagal) to effect energy storage or expenditure. Damage to this hypothalamic control system results in a syndrome of intractable weight gain, termed 'hypothalamic obesity'. A retrospective analysis of weight gain in children with brain tumors established that a younger age at diagnosis, hypothalamic tumor location and degree of damage, tumor histology (particularly those such as craniopharyngioma), dose of radiation to the VMH (> 51 Gy), and presence of endocrinopathy as risk factors for the development of future obesity. These results verify that hypothalamic damage, due to tumor, surgery, or radiation, is the primary cause of obesity in survivors of childhood brain tumors. The pathogenesis of hypothalamic obesity is analogous to an animal model in which the VMH is destroyed or deafferented resulting in anatomic leptin resistance. The brain senses starvation (despite excess adiposity); in response, the VMH decreases sympathetic innervation in order to conserve energy (decreased

locomotion), and increases vagal innervation of the periphery to store more energy in adipose tissue (increased appetite). One other result of this vagal innervation is increased activation of the b-cell, resulting in insulin hypersecretion in response to glucose, which promotes partitioning of energy substrate into adipose tissue. Numerous approaches have been attempted to treat this disorder, including b-cell insulin suppression (octreotide), GLP-1 agonist (exenatide), and bariatric surgery (roux-en-Y, vagotomy), all with variable and inconsistent efficacy. More recently, a triple serotonin-dopamine-norepinephrine reuptake inhibitor (tesofensine) has been approved in adults.

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Session 4

CME4.1

Abstract Unavailable

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CME4.2

'Hypoglycaemia unawareness in type 1 diabetes – lessons learnt'

Rory McCrimmon
University of Dundee, Dundee, United Kingdom

The discovery of insulin and its subsequent mass manufacture transformed the lives of people with type 1 diabetes. Insulin replacement is not, however, without risk and it soon emerged that many individuals with type 1 diabetes experienced iatrogenic hypoglycaemia. Hypoglycaemia in type 1 diabetes has both immediate (cognitive impairment) and longer-term consequences. In this presentation I will focus on the longer-term consequences of recurrent hypoglycaemia and in particular highlight how recurrent hypoglycaemia impacts on those specialised cells in the brain that are critical to the regulation of glucose homeostasis and the counter-regulatory response to hypoglycaemia. In these cells recurrent hypoglycaemia initiates a series of adaptations that ensure they are more resilient to subsequent hypoglycaemia, but this leads to impaired hypoglycaemia awareness and a paradoxical increased risk of severe hypoglycaemia. I will review our current understanding of the underlying mechanism that are responsible for the development of impaired awareness of hypoglycaemia, proposing that this is potentially the result of a process called Habituation. Finally, I will discuss clinical strategies both established and novel that may help restore or prevent hypoglycaemia awareness in type 1 diabetes.

DOI: 10.1530/endoabs.78.CME4.2

Endocrine Main Meeting Sessions

Symposium 1

EMM1.1

'Fertility preservation in boys'

Rod Mitchell
The University of Edinburgh, Edinburgh, United Kingdom

Childhood cancer survival rates have increased dramatically over recent decades and currently > 80% of children with cancer will survive over the long-term. This has resulted in a dramatic increase in the number of young adults experiencing late effects of treatment, including infertility. Ovarian tissue transplantation has recently proven successful for fertility restoration in girls. However, for prepubertal males due to receive gonadotoxic therapy there are currently no clinical options to preserve fertility. Experimental approaches include removing testicular tissue from the patient prior to treatment for cryostorage and subsequent re-transplantation or in-vitro maturation of germ cells. An alternative approach would be to co-administer treatments that can protect the testis from chemotherapy-induced damage. This presentation will describe the current status of clinical and research activity in fertility preservation in prepubertal and adolescent males due to receive gonadotoxic therapies. Website: www.ed.ac.uk/centre-reproductive-health/dr-rod-mitchell E-mail: rod.mitchell@ed.ac.uk Twitter: @RodTMitchell

DOI: 10.1530/endoabs.78.EMM1.1

EMM1.2

Turner Syndrome: Adolescence and Beyond

Joanne McManus
Belfast Health and Social Care Trust, Belfast, United Kingdom

Women with Turner Syndrome should be followed up at a dedicated clinic which provides multidisciplinary input to offer holistic care. Any young person who has been under the care of a specialised paediatric clinic since early childhood will be anxious about the transition to adult services, and this is particularly so for girls with Turner Syndrome. A consultant-based clinic with familiar staff provides reassurance that one person or team is aware of their health needs and can co-ordinate their care. This is usually in the setting of a general endocrinology, specialist gynae endocrinology or menopause clinic. Caring for these young women includes finding a form of suitable HRT to suit individual needs, monitoring blood pressure, thyroid function, liver function and screening for type 2 diabetes. Bone density should be monitored by DEXA scan and lifestyle advice given regarding bone health. If bone density is low, oestradiol levels are useful in assessing compliance with HRT and confirming adequate absorption of oestrogen, while Vitamin D deficiency should also be considered. Due to the high incidence of deranged liver enzymes in women with Turner syndrome, links need to be established with a specialist hepatology clinic. Input from a specialist inherited cardiac disease clinic is also essential with regular follow up for those with previously diagnosed cardiac abnormalities and 5 yearly follow up including cardiac MRI & ECHO even for those with no previously diagnosed abnormalities. This is particularly important for women with Turner Syndrome who wish to pursue assisted conception, who should be advised to discuss any plans for fertility treatment with the doctor who co-ordinates their overall care.

DOI: 10.1530/endoabs.78.EMM1.2

Symposium 2

EMM2.1

GnRH analogue treatment for gender dysphoria

Sabine Hannema
Amsterdam UMC, Amsterdam, Netherlands

An increasing number of transgender adolescents seeks medical care. After careful assessment and in the absence of contraindications, adolescents who have entered puberty, wish treatment and can provide informed consent can be treated with a GnRH analogue (GnRHa). This prevents further development of secondary sex characteristics incongruent with gender identity and provides the adolescent time to consider the option to undergo further gender affirming treatment. Studies on the efficacy and safety of GnRHa treatment will be reviewed. Adolescents who received mental health support plus GnRHa treatment were found to have improved global psychological functioning, reduced or stable emotional and behavioural problems, and reduced suicidality. GnRHa treatment effectively stops progression of breast development and menstrual bleeding in transboys. Those who start treatment in early puberty are less likely to request a mastectomy and, when operated, require less invasive surgery than those who start treatment later on. In transgirls, GnRHa treatment decreases testicular volume and prevents further virilization. However, the smaller size of penis and scrotum resulting from starting treatment in early puberty may affect later surgical options; for instance, penile inversion vaginoplasty may not be possible. The most commonly reported side effects of GnRHa treatment are mild headache and hot flushes. Serious adverse events are rare, but further data are needed on long-term safety. Height SDS decreases and so do bone mineral density z-scores. The great majority of adolescents choose to subsequently start gender affirming hormone treatment. Testosterone and estradiol then stimulate growth and bone mineral accrual, but limited data are available on adult height and bone mass. Another important issue is fertility, which may be compromised in those who choose to undergo further gender affirming treatment. Therefore, options for fertility preservation need to be discussed prior to the start of treatment.

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EMM2.2

Using AMH and Inhibin B Assays in children and young people

Sasha Howard
Queen Mary University of London, London, United Kingdom. Barts Health NHS Trust, London, United Kingdom

The hypothalamic-pituitary-gonadal (HPG) axis is a dynamic endocrine axis, with three main periods of activity - in foetal life, during mini-puberty, and then from puberty into adult reproductive life. Between these periods the axis is dormant and thus difficult to assess, especially in mid-childhood. Inhibin B and anti-Mullerian hormone (AMH) are both markers of gonadal function - of Sertoli cells of the testes and granulosa cells of the ovary - and are very useful investigative tools, both during periods of HPG axis activity and between times. Inhibin B and AMH are being increasing used in paediatric endocrinology to diagnose and measure response to treatment in infants and children with both primary and secondary hypogonadism. Ranges for both of these assays have been defined from birth to adolescence in both healthy and disease cohorts. Serum inhibin-B concentrations in males and females vary during childhood in response to gonadotropin secretion. In boys during the mini-puberty, when Sertoli cells proliferate but do not mature, serum inhibin-B concentrations increase to similar or higher concentrations to those observed in adolescent boys. These levels then decline to lower but readily measurable concentrations until they rise again early in puberty. Undetectable AMH and inhibin B are characteristic of congenital anorchia but may also be seen in males with severe hypogonadotropic hypogonadism. In healthy males, AMH is high in the foetus and newborn, peaking at mini-puberty around two months of age and then decreases by the age of one year. Patients with dysgenetic gonads have low serum AMH while values are elevated in tumours of the Sertoli or granulosa cells. A similar pattern in AMH concentrations during the first months of life has also been reported in infant girls, but the concentrations in girls are significantly lower. AMH plateaus during puberty as sign of androgen action. In girls, concentrations are a marker of ovarian granulosa cell function and are considered a novel marker for follicular reserve. This has importance, for example in Turner syndrome, for assessment of potential reproductive capacity.

DOI: 10.1530/endoabs.78.EMM2.2

Diabetes Professionals Day Sessions

Session 1

DPD1.1

Low Carbohydrate Diets in Type 2 Diabetes: Drug-free remission and hope

David Unwin
Norwood Surgery, Southport, United Kingdom

Dr David Unwin MbChB FRCGP Our GP practice of 9500 people has suffered an eight-fold increase in the number of patients with T2D since 1986. In addition, those affected now develop this condition decades earlier than was the norm back in 1986. A situation replicated all over the developed world. Nationally there are 122,780 children and young adults under the age of 40 years with type 2 diabetes, 1,560 (around 1.3 per cent) are under the age of 19 years. In 2013 our practice decided not to accept this epidemic as inevitable and determined to find novel solutions to this that have resulted in 20% of our entire T2 diabetes population achieving drug-free remission. Saving about £58,000 per year on our diabetes drug budget into the bargain(1). We started with the premise that for most patients a high blood sugar is most often related to something you ate as predicted by the glycaemic index(2) so it seemed logical to cut sugar itself and swap high glycaemic index foods like cereals, rice, potato and pasta with green veg, meat, fish, dairy, eggs, berries and nuts . At 30 months on this lower carb approach, 50% of those adopting this were in remission, also showing significant improvements in renal and liver function, lipid profiles and blood pressure. Over the nine years we have learnt a lot about improving diabetic care for our patients, some of which I hope to share in this presentation.

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2. David Unwin DH, Geoffrey Livesey,. It is the glycaemic response to, not the carbohydrate content of food that maters in diabetes and obesity: The glycaemic index revisited. Journal of Insulin Resistance. 2016;2016;1(1), a8.(https://insulinresistance.org/index.php/jir/article/view/8/11).

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DPD1.2

Low carbohydrate diets in Type 1 diabetes

Frances Hanson
Leeds Children's Hospital, Leeds, United Kingdom

In recent years, Low Carbohydrate Diets (LCD) and Very Low Carbohydrate Diets (VLCD) as management strategies for Type 1 diabetes have been gaining popularity. Whilst now acceptable as an option amongst adults with Type 1 diabetes, the situation in paediatrics is more complicated. While this option is not currently recommended or endorsed by international diabetes experts, paediatric diabetes teams need to be aware of the potential risks of following such restricted diets in the long term, to support children and families who choose to do so. The evidence base is limited, but sufficient to advise enhanced monitoring of physical, biochemical and nutritional parameters, over and above usual annual screening. Discussions should be honest and open to build a positive collaborative relationship with families, for the ultimate best outcome for the child.

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Session 2

DPD2.1

Abstract Unavailable

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DPD2.2

Abstract Unavailable

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Session 3

DPD3.1

Early Detection of Neonatal Diabetes

David McGregor, Tim McDonald & Chris Moudiotis
Royal Devon and Exeter NHS Foundation Trust, Exeter, United Kingdom

Neonatal Diabetes Mellitus (NDM) occurs in the neonatal period and has a very high burden of morbidity and mortality. The incidence is approximately 1:100,000 but reports range from between 1 in 25,000 to 1:500,000 live births. A genetic cause can be found in over 80% of cases. At present, patients with NDM are unrecognised as being seriously ill until hyperglycaemia is at a life-threatening level. An effective method for measuring blood glucose concentrations from Guthrie card samples has been developed that could be incorporated into the current NHS National Newborn Screening (NBS) Programme to detect early hyperglycaemia on day five of life. Retrospective analysis of glucose levels on NBS cards from patients who had a subsequent genetic diagnosis of NDM revealed that the lowest glucose was 8 mmol/l - more than 6 SD above the normal range mean. When asked, parents of these children universally supported the notion of screening that may have detected the condition earlier and avoided such significant illness. Current work has started to validate an assay for glucose using NBS measuring blood glucose levels in 10,000 samples collected during routine NBS in order to determine a normal reference range for NBS samples in the UK population. For a new screening test to be considered acceptable there is a requirement to show that making the diagnosis will prevent avoidable complications or death in a cost-effective manner. As a result further work is being undertaken to evaluate cases of unexplained sudden infant death to ascertain if there are any cases that may have been due to unrecognised NDM. If glucose levels on day 5 become part of the national NBS programme a pathway will be required to ensure that timely assessment, investigation and management are undertaken in a robust and consistent way across the UK.

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DPD3.2

100 years of insulin - is it time for a UK Type 1 diabetes screening strategy?'

Rachel Besser
Oxford University Hospitals NHS Foundation Trust, and University of Oxford

2021 is an important year for diabetes. It is 100 years since insulin was discovered and the first child had their life saved by insulin, turning a death sentence into a chronic condition. Since then, insulin has remained the mainstay of treatment for type 1 diabetes. Outcomes have improved with advances in technology, but outcomes remain suboptimal and, in the UK, around 25% children still present late, in a state of life-threatening diabetic ketoacidosis (DKA). DKA rates have remained unchanged for at least the last 20 years. DKA can cause significant morbidity (cerebral oedema, neurocognitive deficits, shock), and is associated with chronic hyperglycaemia, a predictor of long-term complications. If undiagnosed or complicated, DKA can be fatal. A new diagnosis is typically unexpected and, even in the absence of DKA, is traumatic for children and families, causing depression, problems with adjustment, and stress. It is now possible to identify children with type 1 diabetes before they develop symptoms through measurement of islet-specific antibodies. This offers hope to minimise acute presentations and the rate of DKA at diagnosis. In future it will allow children to access disease-modifying therapies to delay the need for insulin therapy. Since more than 85% newly diagnosed patients do not have a family history of type 1 diabetes, to make an impact on new diagnoses, a general population approach is needed. However, before screening is introduced, the balance of benefit and harm needs to be determined. In this session, I will present the case for national screening for pre-clinical type 1 diabetes and discuss what we need to know before embarking on a national screening strategy.

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Personal Practice Session

DPD4.1

Abstract Unavailable
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DPD4.2

Abstract Unavailable
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Diabetes Main Day Sessions

Symposium 1

DMD1.1

Abstract Unavailable

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DMD1.2

Abstract Unavailable

DOI: 10.1530/endoabs.78.DMD1.2

DMD1.3

Personalising insulin therapy using smart pumps, pens and automated insulin delivery systems

Julia K. Mader
Medical University of Graz, Graz, Austria

People living with diabetes face the daily burden of managing their disease. The ongoing challenge of administering insulin, testing heir glucose and adhering to recommended lifestyle can be overwhelming. Diabetes technology can alleviate some of this burden. However, the technology should be chosen wisely upon preferences and competences of affected people. Insulin pump use has been increasing over the last decades. Insulin pumps re considered a comfortable way to deliver insulin potentially resulting in improved adherence to correction dosesfor elevated glucose, which insulin pen users might skip. There are currently two types of insulin pumps on the market: conventional pumps that require an infusion set to deliver insulin to the infusion site and patch pumps which are directly attached to the site with an adhesive and deliver insulin via an integrated cannula. Smart insulin pens can keep track of the timing of the last insulin dose which helps to avoid insulin dosing errors such as missed doses or injection of double the normal amount. In combination with adequate smartphone apps they can communicate via NFC to directly transfer timing and amount of the injected insulin dose. This is of special interest to people who do not want to use an insulin pump, cannot tolerate the adhesive or do not have access to an insulin pump. Automated insulin delivery systems combine an insulin pump, a continuous glucose monior and an algorithm to steer insulin delivery. Different types of systems are available: integrated systems (all components by one manufacturer), modular systems (components from different manufacturers but are licensed for combined use) and algorithms running as a smart phone app enabling a broader choice of components. Additionally, open-source automated insulin delivery systems where people living with diabetes program their own algorithm and use components of their choice, are currently being used.

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Symposium 2

DMD2.1

Abstract Unavailable

DOI: 10.1530/endoabs.78.DMD2.1

DMD2.2

Psychoeducation and changing behaviour: Knowing how doesn't always mean action

Deborah Christie
University College London Hospital, London, United Kingdom

Not everyone who has the capacity to make positive choices about their lifestyle to care for their health is either ready or willing to make these choices. This lack of interest is frustrating for both family members and healthcare professionals. Many young people living with diabetes understand why caring for diabetes is important but do not see it as a priority and do not have the confidence to put different behaviours into practice. Confidence to change requires the young person to be ready to change, to want to change and to be equipped with a range of skills, resources, and abilities. An initial reaction of health care professionals is to 'educate, educate, educate' by telling people what they need to know and what they need to do. For a significant percentage of our clients however knowing more, knowing how and knowing why does not result in a change in behaviour. Taking a coaching stance with young people invites them to think about what changes they might want to make, when they would want to make them and how they could make them. A coaching stance that incorporates Motivational Interviewing, Solution focussed and Narrative techniques can helping young people explore and resolve ambivalence about behaviour change(1). It requires health care professionals to be thoughtful and skillful and aims to elicit internal motivation to change which can then be used as a prelude to treatment and/or integrated with other treatment approaches. A coaching stance works with ambivalence and resistance that are often particularly challenging to clinicians working with adolescents.

Reference

1. Christie, D. (2008). Dancing with diabetes: brief therapy conversations with children, young people and families living with diabetes. European Diabetes Nursing 5(1), 28-32

DOI: 10.1530/endoabs.78.DMD2.2

DMD2.3

Abstract Unavailable

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Nurses' Day for Endocrine Professionals Sessions

Symposium 1

NEP1.1

Abstract Unavailable

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NEP1.2

Non-medical prescribing: how can you make a difference to your service as a non-medical prescriber?

Kate Davies
Associate Professor, Paediatric Prescribing & Endocrinology, London South Bank University, London, United Kingdom

There are more registered Independent Nurse Prescribers than ever before, and with the advent of paediatric specific prescribing courses and more advanced clinical practice degrees, these numbers will certainly increase. The advantages of practising as an independent nurse prescriber can benefit patient care, improve patient safety, and enhance the overall quality of care a patient receives. This presentation will explore these concepts and introduce advanced clinical skills involved in prescribing, such as focus on clinical assessment, the prescribing process itself, and legal issues surrounding paediatric prescribing practice. It is envisaged that paediatric endocrine nurses listening who hold the qualification – or who wish to study it – will share their experiences from their practice.

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NEP1.3

Abstract Unavailable

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Symposium 2

NEP2.1

Interpretation of abnormal thyroid function tests in children and adolescents

Carla Moran
Beacon Hospital, Dublin, Ireland. University College Dublin, Dublin, Ireland

Thyroid dysfunction is common, and thyroid function tests (TFTs) are amongst the most frequently requested laboratory measurements, both in the adult and paediatric setting. Fortunately, most TFTs are straightforward to interpret and confirm a clinical diagnosis of eu-, hypo- or hyperthyroidism. In most cases, the underlying cause of thyroid dysfunction is readily apparent from clinical findings and standard investigations (e.g. antibody testing, radionuclide scan). In a subset of cases, the cause of thyroid dysfunction can be elusive and/or TFT results can be confusing- either being discordant with the clinical picture or appearing to be incongruent with each other. Causes to consider in such settings include non thyroidal illness, assay interference, genetic disorders (Resistance to Thyroid Hormone alpha or beta, familial dysalbuminaemic hyperthyroxinaemia and others) or environmental causes (e.g. iodine deficiency). In this case-based session, my approach to such patients will be discussed, with particular emphasis on differentiating between possibilities such as assay interference and rare thyroid disorders (such as Resistance to Thyroid Hormone). I will also provide a practical algorithm to the initial investigation and further work up of such patients.

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NEP2.3

Newer treatment options for childhood obesity management

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Childhood obesity is a highly prevalent, chronic, and progressive disease. While lifestyle therapy is the cornerstone of obesity treatment, this intervention is usually ineffective for achieving clinically significant and durable BMI reduction. The limitations of lifestyle therapy stem from the fact that this intervention does not address the underlying pathophysiology of obesity. Anti-obesity pharmacotherapy, in contrast, directly addresses the pathophysiology, thereby enhancing the outcomes achieved with lifestyle therapy alone. Indications for using adjunct anti-obesity medications in the pediatric population include: a) having class 2 or 3 (severe) obesity or b) having class 1 obesity with obesity-related comorbidities. Very few medications are approved for the indication of obesity in children and adolescents. However, recently two medications have been approved: liraglutide, a GLP-1 receptor agonist for obesity in youth ages $\geq$12 years and setmelanotide, a melanocortin-4 receptor agonist, for monogenic obesity due to POMC, PCSK1, and LEPR receptor deficiencies in children ages $\geq$6 years. Furthermore, there are several medications in the pipeline of phase 3 clinical trials. Understanding the role of anti-obesity medications in the management of pediatric obesity is critical for improving the outcomes of this serious disease.

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Oral Communications

Oral Communications 1

OC1.1

Severe hypercalcaemia in Williams-Beuren syndrome.

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Background
Hypercalcaemia is a well-recognised feature amongst children with Williams-Beuren syndrome with a reported incidence between 0-43%[1]. In most cases this is mild however in some, reportedly 6.1% (Sindhar *et al.*[1]) it is severe enough for it to be actionable and cause nephrocalcinosis. We present 2 cases of severe hypercalcaemia requiring treatment with bisphosphonates.
Case 1
A 16 month old male admitted following routine bloods due to developmental delay and recently having been more unsettled. Bloods revealed acute kidney injury (AKI) with urea 15.2 mmol/l and creatinine 73 umol/l with hypercalcemia of 3.26 mmol/l. He was commenced on 200% hyper-hydration with furosemide cover. His calcium level remained high at 3.14 mmol/l therefore his IVF were stopped and he was managed with a pamidronate infusion. The dose was discussed with the renal team given his AKI and hypertension (132/88). He responded well as his calcium fell to 2.6 mmol/l. He required a further pamidronate infusion 2 weeks later as his calcium level had risen to 3 mmol/l. Both infusions were well tolerated.
Case 2
17 month old male with known Williams-Beuren syndrome admitted with vomiting, cough & lethargy. Bloods showed calcium of 3.5 mmol/l. Parents felt he had low tone, poor appetite and constipation. Due to difficult IV access he was managed initially with increased oral fluids which improved calcium to 2.67 mmol/l however his calcium increased further to 4.4 mmol/l. He received hyper-hydration and furosemide. After 48 hrs of hyper-hydration his adjusted calcium remained high (3.04 mmol/l) therefore he received one dose of IV pamidronate. He had no side effects or acute phase reaction and calcium normalised to 2.46. Both cases were managed with a low calcium diet and USS showed evidence of medullary nephrocalcinosis.
Conclusion
Severe and refractory hypercalcaemia is uncommon but potential harmful condition seen in Williams-Beuren syndrome. Early recognition of the condition and appropriate treatment are essential to optimise outcomes in such patient group. We have also shown that pamidronate has been well tolerated in the presence of AKI.

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OC1.2

Two cases of functioning adrenocortical tumours secondary to TP53 variants

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Introduction
We report the complexities in the management of two patients with functioning adrenocortical tumours (ACTs), presenting with features of androgen and cortisol excess, secondary to *TP53* variants.
Case report
Patient 1 presented with androgen excess (P1, TVs 2mls, penis 10 cm) aged 18 months. He was a known carrier of a maternally inherited *TP53* variant. Adrenal androgens were elevated, with a DHEAS level of 86 umol/l (0.0-1.9 umol/l). A urine steroid profile (USP) indicated an ACT. The diagnosis was confirmed by MRI, following a normal abdominal ultrasound. Patient 2 presented aged 19 months with virilisation (P1, TVs 3-4mls, penis 6 cm) and signs of cortisol excess (Cushingoid facies, hypertension and growth failure). He had a family history of cancer predisposition. He similarly had elevated adrenal androgens, with a DHEAS level of $>$ 30 umol/l and a USP indicative of an ACT. His 24-hour urine free cortisol results were elevated, with a suppressed 9am ACTH and absent cortisol circadian rhythm. Patient 2 required amlodipine for pre-operative blood pressure stabilisation. Early open surgical resection was performed for both. Histology reported an ACT with no evidence of malignancy for Patient 1 and an ACT of uncertain malignant potential for Patient 2. DHEAS levels rapidly decreased to 0.1 umol/l for both patients. Patient 1 discontinued glucocorticoids after six months following contralateral adrenal gland recovery. Patient 2 remains on glucocorticoids and mineralocorticoids. Both continue under close clinical, biochemical and radiological surveillance. Behavioural management is a significant challenge. A *TP53* variant of uncertain significance has since been identified in Patient 2.
Discussion
ACTs are rare in children, but may occur in genetically susceptible individuals. Genetic investigation and counselling must be offered to families with a positive TP53 mutation and irradiation should be avoided if possible. Abdominal ultrasound is the first line radiological investigation however a normal scan does not exclude ACT. For functioning ACTs, DHEAS is a useful post-operative tumour marker for residual disease detection. Recovery time of the contralateral adrenal axis varies. Long-term follow-up to include developmental assessment and behavioural management is essential, given the impact of adrenal disorders on the developing brain.

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Oral Communications 2

OC2.1

Pitfalls and challenges in the diagnosis and management of Cushing's disease in children: An interesting case

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Introduction
Cushing's disease (CD) is a very rare cause of obesity in children. Typical features seen in adults with CD may be absent and clinical investigations may not give a definitive diagnosis. We present a case of CD, highlighting the challenges of diagnosis and the dilemmas encountered in managing such patients.
Case report
A ten-year-old girl was referred with a five-year history of weight gain. At presentation BMI was $+3.66$ SD and she had a plethoric complexion. Despite signs of puberty, height velocity was 4 cm/yr. Investigations including repeated 24 h urinary free cortisols (UFC) and a midnight cortisol of 515nmol/l suggested increased cortisol secretion. A low-dose dexamethasone suppression test (DST) however demonstrated suppression of cortisol ($<$22nmol/l), with subsequent 48hr DST showing 48hr cortisol $<$22nmol/l, ACTH 36.7ng/l. A 3mm lesion in the pituitary gland, consistent with a pituitary microadenoma, was identified on MRI scan, therefore Cushing's disease was diagnosed. The patient underwent a transsphenoidal resection of her microadenoma. Surgical evaluation and MRI imaging suggested complete resection. Post-operative cortisol levels fell to 126-231nmol/l in a 24 hr period. Clinically the patient lost weight, height velocity improved and she became less plethoric. One year later however, height velocity slowed and weight loss tailed off. Investigations initially showed an inconclusive picture. Over time, 24 h UFC and salivary cortisol and cortisone measurements became persistently elevated, consistent with recurrence of CD. Treatment with metyrapone was instigated, using cortisol day profiles to titrate the dose and monitor for adrenal axis suppression. Subsequently hydrocortisone was added to the block and replace regime. On treatment the patient has regained her normal appearance, benefited from an improved quality of life and achieved significant weight loss (BMI currently 91st-98th centile).
Conclusions
This case highlights a number of important learning points in diagnosing and managing CD. Linear growth failure in association with obesity is a key feature of CD in children and monitoring of growth parameters may alert the clinician to disease recurrence. We will discuss the role of post-operative cortisol measurements in predicting likelihood of disease recurrence, the challenges of surgical management and the role of medical therapy.

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OC2.2

Two cases of McCune-Albright Syndrome with multisystem involvement

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Introduction
McCune-Albright syndrome (MAS) is a rare disorder characterized by skeletal lesions, skin hyperpigmentation, and hyperfunctioning endocrinopathies. It is due to the postzygotic gain-of-function mutations in *GNAS1*, which encodes the α-subunit of the Gs signaling protein.

Case 1
A 13 year old boy presented initially with a femur fracture at the age of 5.5 years following minor injury. Café au lait patches were noted. Bone scan and skeletal survey revealed multiple FD involving the skull, long bones and pelvis. *GNAS1* mutation analysis was negative. Peripheral precocious puberty was identified at the age of 6 years which subsequently trigged central puberty needing treatment with a combination of Bicalutamide, Anastrazole and GnRH analogues. He was noted to have asymmetrical testes with bilateral microlithiasis and the tumours markers were negative. He was tall with increased height velocity, high IGF1 and IGFBP3 and non-suppressed growth hormone to OGTT which was managed with monthly Lanreotide injections. He was also diagnosed with hypophosphatemic rickets with elevated FGF23 (140RU/ml), which was managed with phosphate supplements and 1α Calcidol. Prolactin levels have been persistently high but he is asymptomatic. He is currently 13 years old and has completed the treatment for early puberty and growth hormone excess. Management of hypophosphatemic rickets continues to be a challenge and Burosumab treatment is being considered.
Case 2
A 1.5year old baby girl presented with episodic vaginal bleeding since the age of 3 months, associated with breast development. Café au lait patches were noted and *GNAS1* mutation was identified. Estradiol was high with suppressed LH and FSH. Cystic lesions with multiple daughter cysts and a 4.7 cm pear shaped uterus with endometrial thickness of 2.2mm were noted in the ultrasound. She was started on Letrozole with good clinical effect and subsequent imaging revealed regression of ovarian cysts with reduction of uterine and ovarian size.
Conclusion
MAS could present with a wide range of phenotypic features and could pose challenges in management especially when there is multisystem involvement. A close surveillance for evolving skeletal and extra skeletal complications is necessary.

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Oral Communications 3

OC3.1

Rapid-Onset Obesity, Hypothalamic Dysfunction, Hypoventilation, and Autonomic Dysregulation Syndrome (ROHHAD-NET): Case series & learning points

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Introduction
Rapid-onset obesity with hypoventilation, hypothalamic dysfunction, autonomic dysregulation, and neuro-endocrine tumour (ROHHAD-NET) is a rare syndrome associated with high morbidity and mortality. With no clear aetiology, diagnosis is based on constellation of clinical features. Management is supportive, although various immunosuppressive agents have been used with variable benefits. We present 3 cases of ROHHAD with heterogeneous presentations and clinical features.
Case 1
The patient presented at 6 years with sweatiness, tiredness and weight gain (BMI SDS +2.45). She had hyperprolactinaemia (3000mIU/l; NR<699), central diabetes insipidus (DI) with recurrent asymptomatic severe hypernatraemia (sodium up to 185 mmol/l), growth hormone (GH) deficiency and central hypothyroidism. MRI pituitary was normal. She has impaired glucose tolerance. A benign ganglioneuroma was found on MRI spine at age 13 along with an incidental finding of gut malrotation (requiring surgical correction) and polysplenia. Sleep studies remained normal until age 14 when she developed central hypoventilation requiring nocturnal BiPAP.
Case 2
The patient presented in cardio-respiratory arrest at 4 years of age following a 6-month period of rapid weight gain (BMI SDS +3.1). A sleep study showed central hypoventilation requiring nocturnal BiPAP. She was diagnosed with central DI, hyperprolactinaemia (1700mIU/l) and GH deficiency. MRI pituitary, abdomen and pelvis were normal. She had abnormal glucose handling on OGTT (2 h blood glucose 12.2 mmol/l; NR <11.1) but normal HbA1c (33 mmol/mol) and no features of diabetes.
Case 3
The patient presented aged 4 years with hyperphagia and rapid weight gain over a 7-month period (BMI SDS +3.83). She has hyperprolactinaemia (1104mIU/l; NR <699) central hypothyroidism, and intermittent hypernatraemia. MRI pituitary and whole body were normal. Aged 8 years, a sleep study to investigate daytime somnolence demonstrated central hypoventilation and nocturnal BiPAP was commenced.
Discussion
All three patients had obesity, central hypoventilation and hypothalamic-pituitary (HP) dysfunction. High prolactin was a consistent feature of HP dysfunction. Central hypoventilation and NET may not be present initially but may develop over time. Therefore, regular sleep studies and screening for NETs are required. A high degree of clinical suspicion of ROHHAD is needed in patients with early-onset obesity and HP dysfunction/hyperprolactinaemia with no structural pituitary abnormality.

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OC3.2

Variable responses to sulfonylurea treatment in siblings from the same family with monogenic diabetes due to HNF1A mutation

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Background
Maturity onset diabetes of the young (MODY) is characterized by autosomal dominant inheritance, onset before 25 years of age, absence of β-cell autoimmunity, and sustained pancreatic β-cell function. *HNF1A* mutations account for 70% of MODY cases. Patients with *HNF1A* MODY are sensitive to sulfonylureas (SU) and can maintain optimal glycaemic control with SU rather than insulin. We describe 2 siblings from the same family with *HNF1A* MODY and variable SU responses.
Cases Patient 1
This male patient of Sudanese origin was diagnosed with diabetes at 13 years of age in Sudan and commenced on insulin. A review in the UK (after family migration) revealed a strong family history of young-onset diabetes from the maternal side and no development of ketones or becoming unwell despite days without insulin. The C-Peptide was 1090pmol/l with negative diabetes auto-antibodies and a glycated haemoglobin (HbA1C) of 112 mmol/mol. He showed no clinical features of insulin resistance and BMI was 28 kg/m^2 (SDS: +2.01) Insulin was commenced and his HbA1C improved to 51 mmol/mol. Subsequent genetic testing confirmed MODY due to a pathogenic missense variant in *HNF1A* p.(Pro379Arg). Following this, his insulin was stopped and gliclazide commenced. Despite maximal dosing (80 mg BD) and ensuring compliance, the blood glucose (BG) showed no significant response (average BG:10-14 mmol/l) with deterioration of HbA1C (94 mmol/mol). Subsequently, his insulin has been restarted.
Patient 2
The 14 year old female sibling of patient 1, developed osmotic symptoms (polydipsia) and random BG testing both at home and with her GP was consistently high (13 mmol/l). She had an increased BMI of 47 kg/m^2 (SDS: +4) without clinical features of insulin resistance. The HbA1C was 85 mmol/mol, diabetic auto-antibodies were negative and the c-peptide was 2080pmol/l. Genetic testing confirmed the same mutation *HNF1A* p.(Pro379Arg). Gliclazide was commenced at 20 mg OD, increased to 40 mg OD and insulin was stopped. The BG remains between 8-9 mmol/l with an improvement of HbA1C to 63 mmol/mol.
Discussion
The above cases describe unusual variable responses to SU in siblings from the same family with the same mutation. The precise reason for this is currently unclear but may be secondary to a potential decline in β-cell function.

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Oral Communications 4

OC4.1

Dominant mutations in CCDC141 are found by ehole rxome dequencing to be a common cause of self-limited delayed puberty

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Puberty is a fascinating transition period in the mammalian lifespan, but the biological control of pubertal timing remains poorly understood. Developmental abnormalities of the gonadotropin-releasing hormone (GnRH) neuronal network have been shown to be responsible for disorders of pubertal timing, in a spectrum of conditions ranging from idiopathic hypogonadotropic hypogonadism (IHH) to self-limited delayed puberty. We hypothesized that important regulators of pubertal timing could be identified through interrogation of genetic defects in

GnRH pathways in patients with pubertal delay. We analyzed whole exome sequencing data from 197 individuals, from 100 pedigrees from our cohort with familial self-limited delayed puberty. We applied a virtual panel of gene pathways related to GnRH development and function to filter the dataset returned from this whole exome sequencing study ($n = 12$). From this analysis we identified six rare predicted deleterious variants in the gene *Coiled-Coil Domain Containing 141* (*CCDC141)* in 26 individuals from 8 families. Previous studies reported that homozygous or compound heterozygous mutations of *CCDC141* cause Kallmann syndrome and IHH, due to impaired GnRH neuronal migration. All probands who were found to carry heterozygous missense variants showed typical clinical manifestations of SLDP. Homology modelling predicted the pathogenicity of all 6 of these variants. Our *in vitro* studies demonstrated that CCDC141 mutant proteins have atypical subcellular localisation associated with abnormal distribution of acetylated tubulin. Moreover, expression of mutant proteins in a cellular assay resulted in a significantly delayed cell migration. These data identify mutations in *CCDC141* as a frequent cause of SLDP. The mis-localisation of acetylated tubulin and reduced cell migration seen with mutant CCDC141 suggests a role of the CCDC141-microtubule axis in GnRH neuronal migration, with defects impacting the timing of puberty.

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OC4.2

Pseudohypoparathyroidism type 1A and 1B: presentation, phenotypes and phenotype-genotype associations

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Background & Objective
Pseudohypoparathyroidism (PHP), a heterogeneous condition, classically causes parathyroid hormone (PTH) resistance. PHP1a is caused by heterozygous inactivating mutations on the maternally derived *GNAS* allele. PHP1b results from methylation defects at the GNAS imprinted gene cluster, which are either sporadic, or familial, normally associated with maternally inherited intragenic STX16 deletions. We investigated the presentation, phenotype, and phenotype-genotype associations of a large PHP cohort.
Method
Casenote review of PHP patients at two UK tertiary centres.
Results
59 patients were identified, from 45 kindreds; 33 with PHP1a, 26 with PHP1b. PHP1a patients (58% female, 70% White), presented at 3.9+/-6.0 years. 11 presented with hypothyroidism; predominantly with congenital hypothyroidism ($n = 8$), including 2 with thyroid agenesis. Others mainly presented with hypocalcaemia or were identified by familial testing. There was frequently significant delay from first presentation to diagnosis. Currently, only 72% have PTH resistance but 94% have TSH resistance/hypothyroidism. 6 have GHRH resistance, 2 delayed puberty, 1 precocious puberty. 40% of patients older than 12 years ($n = 20$) have type 2 diabetes (T2D) or severe insulin insensitivity (average weight only +1.66 SDS). 15 PHP1a patients with *GNAS* missense variants are of similar weight SDS but shorter ($P = 0.004$) than those with other variants; they presented later and fewer have PTH resistance (33% vs. 100%) or ossifications. Two patients with frameshift/splicing mutations have progressive osseous heteroplasia (POH). The PHP1b cohort (54% female, 46% White), presented later at 9.4+/-6.5 years ($P < 0.05$); two thirds with hypocalcaemia. They are taller ($P < 0.0005$) than PHP1a patients and PTH resistance is more frequent (92%). 32% have TSH resistance. 10 patients with STX16 deletions are heavier ($P = 0.008$), not shorter, than those with sporadic methylation defects. Similar numbers take levothyroxine and alfacalcidol.
Discussion
We describe one of the largest PHP cohorts, reporting notable findings. 25% of PHP1a patients presented with congenital hypothyroidism. POH is not solely seen with paternally derived *GNAS* mutations but can occur in PHP1a. T2D is commonly seen in young PHP1a patients. Missense variants might cause a milder phenotype, without PTH resistance. A third of PHP1b patients have TSH resistance, with little phenotypic difference between sporadic and familial methylation defects.

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OC4.3

Growth hormone receptor 6Ω pseudoexon activation: a novel cause of severe growth hormone insensitivity

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Context
Severe or 'classical' growth hormone insensitivity (GHI) is characterised by extreme short stature, dysmorphism and metabolic anomalies. It is caused by homozygous or compound heterozygous mutations of the Growth Hormone Receptor gene (*GHR*). Genetic analysis traditionally focuses on the exonic regions of gene(s). The non-coding regions of the genome may harbour numerous disease-causing mutations that are not well recognised or understood.
Objective
Identification of the genetic cause of growth failure in 3 'classical' GHI subjects. Assessment of identified novel 6Ω pseudoexon *GHR* variant.
Design
Genetic variants of interest were identified using our targeted whole genome gene panel and filtered using our custom bioinformatics pipeline. *In vitro* splicing assays were performed to confirm aberrant splicing. Patient fibroblast analysis was performed to determine the presence of the *GHR* 6Ω pseudoexon in cDNA transcripts. A 6Ω pseudoexon *GHR* vector created by Gibson assembly assessed the functional consequences of the novel inclusion.
Results
We identified a novel homozygous intronic *GHR* variant (g.5:42700940T>G, c.618+836T> G), 44bp downstream of the previously recognised intronic 6Ψ *GHR* pseudoexon mutation, in the index patient. In the second kindred, two siblings were also found to harbour this novel intronic 6Ω pseudoexon *GHR* variant in compound heterozygosity with the known *GHR* c.181C>T (R43X) mutation. RT-PCR of patient fibroblasts demonstrated the presence of the 6Ω pseudoexon transcript in patient cDNA. *In* vitro splicing analysis confirmed inclusion of a 151bp mutant 6Ω pseudoexon not identified in wild-type constructs. Inclusion of the 6Ω pseudoexon causes a frameshift resulting in a non-functional truncated GHR lacking the transmembrane and intracellular domains. The 6Ω pseudoexon Gibson construct demonstrated extracellular accumulation of the mutant, truncated GHR protein and diminished activation of STAT5B signalling following growth hormone stimulation.
Conclusion
Novel *GHR* 6Ω pseudoexon inclusion results in complete loss of GHR function consistent with a severe GHI phenotype. This represents a novel mechanism of GHI and is the first deep intronic variant identified causing severe postnatal growth failure. The two kindreds originate from Campania, Southern Italy, implying common ancestry. Our findings highlight the importance of studying variation in deep intronic regions as a cause of monogenic disorders.

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OC4.4

Does Inflammation Underpin Polycystic Ovary Syndrome (PCOS)? A Proteomic Approach to Novel Non-Invasive Biomarker and Pathway Discovery in Adolescent PCOS

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Background and Methods
PCOS is common and associated with significant comorbidity. Yet, its pathogenesis is complex and poorly understood. We have developed new methods for deep phenotyping discovery proteomic profiling of urine to identify disease mechanisms and novel non-invasive biomarkers for PCOS in adolescents. We undertook proteomic analysis (nano 2D-LC-QTOF MS^e) on a subset of 15 samples from a longitudinal PCOS cohort of 40 participants. We compared the urinary proteome of adolescents with PCOS ($n = 6$), controls ($n = 6$), and insulin resistance (IR) ($n = 3$), to identify markers of PCOS as distinct from those of IR. Subsequently, we ran a novel assay of 96 pro/anti-inflammatory associated proteins.
Results
In the discovery proteomic analysis, we identified 3,793 proteins, of which, 314 were significantly and differentially expressed ($P < 0.05$) in the PCOS cohort in comparison to healthy controls, and 397 in the PCOS vs. IR analysis. Of these, 66 proteins are potential novel biomarkers for PCOS – being differentially expressed in the PCOS cohort in comparison to both controls and IR. Gene ontology and bioinformatic Ingenuity Pathway Analysis (IPA) revealed that many proteins were mediators of complement, coagulation and apoptosis cascades or pro-inflammatory cytokines. Almost half of all significant biological pathways (10/23; 43%) were related to inflammatory/immunological responses and the thrombotic/fibrinolytic systems, and the *inflammatory response* was the most significant biological process associated with PCOS ($P < 0.001$). To validate these findings, we used an in-house, multiplexed and targeted proteomic assay of known inflammatory markers. This panel allowed us to identify and quantitate 80 of 96 pro/anti-inflammatory proteins in our cohorts. Multivariate analysis of all inflammatory proteins revealed clear separation between the three cohorts. Univariate analysis revealed four significantly different proteins between PCOS vs. control cohorts, six proteins between PCOS vs. IR cohorts, and one significant protein between all three cohorts.
Conclusions
We have utilised non-invasive matrices to map the proteome in adolescent PCOS and identified 66 potential novel biomarkers, providing greater insight into its molecular underpinnings. Our initial findings suggest inflammation is a major contributory factor in the pathophysiology of PCOS, which we corroborated through targeted assays. Future studies include proteomic analysis of the entire longitudinal cohort.

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OC4.5

The biochemical evaluation of Metabolic Bone Disease of Prematurity (MBDP) in a high-risk population

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Background
MBDP describes inadequate mineralisation of bones in the preterm infant. Traditionally, neonatologists have used a raised ALP and low phosphate to diagnose MBDP, with phosphate supplements as first-line treatment. An alternative management approach, published by Chinoy *et al* (2019), recommended PTH and vitamin D in the routine work-up.
Objectives
We undertook a review of data across two neonatal intensive care units:
- to report the incidence of MBDP defined by biochemical markers on routine blood testing of high-risk infants
- to determine the frequency of PTH and vitamin D measurement in infants meeting biochemical criteria for MBDP
- to report the incidence of MBDP related fractures

Methods
Infants <30 weeks gestation or <1500 grams, admitted for >28 days between 01/01/2015 and 31/12/2019 were included. Blood results for the duration of their admission were reviewed. Biochemical MBDP was defined as ALP >500IU/l and either phosphate <1.8 mmol/l or corrected calcium <2.2 mmol/l. Infants with a MBDP related fracture were identified from BadgerNet.
Results
A total of 809 infants were identified over a 5-year period; 424 met biochemical criteria for MBDP (52.4%). PTH was measured in 30 infants (7%); 24 had a maximum level >10 pmol/l. Vitamin D was measured in 136 infants (32%); 3 had a level <25 nmol/l, 28 had a level 25-50 nmol/l and 105 had a level >50 nmol/l. There were 4 documented fractures (1 humeral and 3 rib fractures).
Conclusions
PTH and vitamin D were measured in a minority of infants meeting biochemical criteria for MBDP. When it was measured, 80% had a raised PTH level, which would favour calcium supplementation over further phosphate provision. Treatment could be improved by targeted measurement of these markers. Whilst the majority of infants were vitamin D replete, a significant minority may have benefited from supplementation. The documented incidence of fracture related to biochemical MBDP was 1%. This suggests few babies suffered immediate severe effects of their MBDP, which may mean that the implementation of new guidance is met with scepticism. However, further research is required to explore the effects of MBDP on these infants' short- and long-term outcomes.

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OC4.6

The management of adrenal cell carcinoma in the United Kingdom at a single centre: a 25 year experience

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Background
Adrenal cortical carcinoma (ACC) in children is a rare and aggressive disease. Further characterisation of the presenting features and biochemical markers are needed to support earlier diagnosis. Refractory hypertension related to high cortisol concentrations at presentation, and post-operative decrease in cortisol can be challenging to manage. Focus on endocrine management has not been previously described.
Case Series
34 patients (age 2 weeks–10 years (y), median 2.35y, 17 female) presenting with an ACC (1996-2021). Patients were either low ($n = 15$), borderline ($n = 2$), or high ($n = 17$) malignancy risk based on histology and tumour size. The most frequent presentations included virilisation ($n = 29$), hypertension ($n = 20$), cushingoid appearance ($n = 15$), and rarely gynaecomastia. 38% patients had an identified genetic mutation, either *TP53* ($n = 10$, $n = 8$ high risk), or a mutation associated with Beckwith Wiedemann syndrome ($n = 3$, borderline $n = 1$ or high risk $n = 2$). Elevated cortisol concentrations were seen in most patients, with loss of circadian rhythm in one third. Androgen concentrations were frequently elevated (Androstenedione 88%, DHEA-S 61%, Testosterone 93%). Urine steroid profile pre-surgery revealed elevated androgen and cortisol metabolites. Refractory hypertension necessitated the use of metyrapone ($n = 3$) and ketoconazole ($n = 3$). All patients underwent surgical resection, a laparoscopic approach evolving over time, and 32% received adjuvant chemotherapy. Elevated biochemical markers resolved post-surgery, and most patients received intravenous hydrocortisone infusions post-operatively. All were discharged on hydrocortisone replacement (10 mg/m^2/day; duration 0.1-8y, median 1y). Those treated with mitotane ($n = 8$) required a higher dose (15-17 mg/m^2/day), with added fludrocortisone ($n = 3$), and thyroxine ($n = 2$). The mortality rate was 32% in this cohort, although comorbidities were contributing factors in at least two patients.
Conclusion
This series describes the most frequent presentations in this rare and aggressive disease, and highlights the essential role of genetic diagnosis in influencing disease progression and treatment. Our practice has evolved to include post-operative intravenous hydrocortisone infusion in all patients to mitigate the effect of the rapid fall in cortisol. The duration of hydrocortisone requirement in this cohort was highly variable. Future research is required into the use of newer agents such as pasireotide or mifepristone to decrease cortisol concentrations in those with refractory hypertension, as they may have fewer side-effects and reduce morbidity.

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OC4.7

The use of urinary steroid profiles in monitoring therapy in children with 21-hydroxylase deficiency – results from the CAH-UK cohort study

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Introduction
Monitoring glucocorticoid (GC) replacement in patients with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) remains challenging. There are disease-specific patterns in the plasma and urinary steroid profiles in 21OHD, a key role being played by the 11-oxygenatedC19 androgens.
Aim
To explore the urinary steroid profile in 21OHD in relation to treatment and plasma steroids.
Methods
Participants consisted of 91 patients with 21OHD on hydrocortisone therapy (age 12.5 $\pm$ 2.8 years, 53% females), from 14 UK centres. Urinary steroids (24-hour profiles), adjusted for body surface and $\log_{10}$-transformed, were analysed in relation to clinical data and morning plasma steroid panels. Urinary steroids were analysed individually and grouped as cortisol, 17-hydroxyprogesterone (17OHP) and androgen metabolite sums. The 11 β-hydroxysteroid dehydrogenase (HSD-11 β) activity was calculated as (5α-tetrahydrocortisol + tetrahydrocortisol)/ tetrahydrocortisone.
Results
Urinary 17OHP and androgen metabolites correlated well with plasma 17OHP, androstenedione, testosterone, 11-hydroxyandrostenedione and 11-ketotestosterone. The best correlations were found for urinary pregnanetriolone with plasma 17OHP ($r_s = 0.767$, $P < 0.001$) and urinary 11-hydroxyandrosterone with plasma 11-hydroxyandrostenedione and 11-ketotestosterone ($r_s = 0.829$, $P < 0.001$ and $r_s = 0.736$, $P < 0.001$). Urinary pregnanetriolone, 11-hydroxyandrosterone, 17OPH and androgen sums were significantly different (Kruskal-Wallis, $P < 0.001$) between patient subgroups of <12, 12-36 and >36 nmol/l plasma 17OHP, classified as suppressed, good control and under-treated, respectively. Urinary cortisol metabolites correlated positively with 17OHP and androgen metabolites ($r_s = 0.634$, $P < 0.001$ and $r_s = 0.603$, $P < 0.001$), suggesting lack of androgen suppression despite using high GC doses in some patients. A multivariate linear regression showed an increase of the urinary cortisol metabolites with the GC dose, when adjusted for the HSD-11 β activity ($R^2 = 0.288$, $P < 0.001$). Male patients were receiving higher GC doses ($P = 0.031$) and had higher urinary cortisol metabolites compared to females ($P = 0.020$). Patients 12 years and older had higher urinary cortisol ($P = 0.025$), 17OHP ($P = 0.024$) and androgen ($P = 0.002$) metabolites compared to younger children.
Conclusions
The close correlation of urinary 17OHP and androgen metabolites with plasma biomarkers, including 11-oxygenated androgens, support their role as markers of therapy control. Given their relationship with the GC dose, cortisol metabolites may be used to monitor compliance and toxicity. These findings support the use of urinary steroid profiles as an adjuvant non-invasive test in monitoring CAH.

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OC4.8

Destination outcome of 1151 gender variant young people presenting to paediatric endocrinology clinics in England and Wales since 2008.

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Introduction
The destination of young people referred from the NHS Gender Identity Development Service (GIDS) to the two paediatric endocrine centres covering England and Wales has not been analysed previously.
Methods
1151 young people identifying as gender variant were referred from GIDS for an endocrine opinion: 827 patients to University College London Hospital (UCLH) from 2008; 324 to Leeds Children's Hospital (LCH) from 2013. Outcomes were not known for 24/1151 patients (2.1%). 8 have emigrated.
Results
Of those continuing to identify as transgender:
867 (75.3%) were discharged to adult gender identity clinics (GICs). 166 (70.3%) were <16 yr and 701 (76.6%) were >16 yr at the time of referral to the endocrine clinics. 989 (85.9%) continued identifying as gender variant, most with NHS support. 38 (3.3%) opted for non-NHS services. 8 (0.7%) were either assessed as not competent or had significant overlying mental illness which prevented endocrine intervention despite continuing to identify as transgender.
Of those ceasing to identify as transgender:
59 (5.1%) ceased identifying as transgender either after referral or after the first clinic appointment. A higher proportion were in the <16 yr group (6.4%) compared with >16 yr group (4.8%). 58 (5.0%) young people ceased treatment either with a GnRH analogue or cross sex hormones (CSH) and reverted to birth gender identification. A higher proportion were in <16 yr group (8.5%), than the >16 yr group (4.2%). Of those <16 yr, 6.8% ceased after GnRHa and 1.7% after CSH. In the over 16s, 3.6% ceased after GnRHa and 0.6% after CSH.
Conclusions
- Of those referred to paediatric endocrine clinics, 86% continued to identify as transgender, 75% seeking ongoing care through NHS GICs.
- 5.1% ceased identifying as transgender after an initial consultation prior to any endocrine intervention. A higher proportion were in the <16 yr group (6.4%) compared with >16 yr group (4.8%).
- Overall 58 (5.0%) of young people ceased treatment either with GnRHa or CSH and reverted to identify with birth gender. There was a higher proportion in the <16 yr group (8.5%) compared with the $>$ 16 yr group (4.2%).

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OC4.9

The use of Liraglutide in the treatment of childhood obesity

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Introduction
Childhood obesity remains a major health concern and there are a number of serious complications associated with it. These include type 2 diabetes mellitus (T2DM), obstructive sleep apnoea (OSA), idiopathic intracranial hypertension (IIH) and non-alcoholic fatty liver disease (NAFLD). Glucagon-like peptide 1 (GLP-1) therapy has shown promising results for weight loss in adults and has recently been approved for the use in the treatment of childhood obesity for adolescents aged 12 years and over.
Method
Adolescents with severe obesity attended a dedicated multidisciplinary team (MDT) weight management clinic. Each patient had significant complications secondary to obesity, which included T2DM, insulin resistance, IIH, OSA, dyslipidaemia, hepatic fibrosis, delayed puberty and depression. Liraglutide, a once daily subcutaneous injection, was commenced at a dose of 0.6 mg and increased, if required, to a maximum dose of 3 mg. The patients were reviewed by the MDT every two weeks.
Results
Seven patients completed a three-month course of Liraglutide and three of these continued to complete six months in total. The mean age at the start of the treatment course was 14.9 years (range:13-16 years) and all patients were female. Mean percentage weight loss was 4.2% (1.2-9.7%) and 5.8% (4-8.2%) at 3 and 6 months, respectively. Significant weight loss (5.3 kg, 95%CI 1.93-8.78, $P = 0.009$) and significant reduction in body mass index [BMI] (2.09 kg/m^2, 95% CI

0.97-3.20, $P = 0.004$) was noted at 3 months of treatment. This further continued with weight loss (6.9 kg, 95% CI 1.33-12.53, $P = 0.033$) and BMI reduction (2 kg/m^2, 95% CI 0.06-3.94, $P = 0.047$) being significant at 6 months of treatment. There were no side effects reported during the treatment courses. Resolution of IIH and steatohepatitis were noted following weight loss in two patients.
Conclusion
These are promising results showing significant weight loss and BMI reduction in adolescents over three and six months of liraglutide treatment, alongside regular support from a dedicated MDT. This intervention has potential to help and improve significant complications secondary to childhood obesity.

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Oral Communications 5

OC5.1

Evaluating UK Referral Criteria for Children with Short Stature in a Tertiary Paediatric Endocrinology Centre

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Background
Childhood growth monitoring aims to identify growth failure and detect underlying pathology. According to UK guidance, height <-2.7 standard deviation score (SDS) (<0.4th percentile) is used as the referral threshold. Additional referral criteria include height deficit (HSDS-target height SDS) <-2.0 and height velocity (HV) SDS <-1.3. Lack of routine HV and mid-parental height calculation, combined with stricter cut-offs compared to other European countries means that UK screening to detect growth disorders is suboptimal.
Methods
Retrospective review of children referred with short stature to Paediatric Endocrinology clinics at the Royal London Children's Hospital between 2016-2020. Demographics, HSDS, HVSDS and Height-THSDS were recorded at the time of referral.
Results
143 patients were referred with short stature (SS). 51 (36%) patients had pathological SS; 28 with primary growth failure: genetic disorder ($n = 6$), SGA ($n = 21$), SHOX ($n = 1$) and 23 with secondary growth failure: GHD ($n = 17$), GH-IGF axis disorder ($n = 4$), coeliac disease ($n = 1$) and hypothyroidism ($n = 1$). 15 (10%) patients remain short and under investigation with no identified pathology. 48 (34%) had non-pathological SS: FSS ($n = 30$), CDGP ($n = 18$). 29 (20%) patients did not have short stature (HSDS >2.0 and <1.6 SDS below TH). Height SDS and height-THSDS were significantly lower in the pathological SS group ($n = 66$) vs the non-pathological SS/normal stature group ($n = 77$) (-2.67 $\pm$0.82 vs -1.97 $\pm$0.70; $P < 0.001$ and -2.07 $\pm$1.02 vs -1.06 $\pm$0.99; $P < 0.001$, respectively). HV SDS did not differ between the groups (-0.49 $\pm$2.71 vs -0.16 $\pm$2.82; $P = 0.49$). The sensitivity and specificity to detect pathology was 41% and 83% for height SDS <-2.7, 48% and 83% for HSDS-THSDS <-2.0 and 33% and 68% for HVSDS <-1.3.
Conclusion
Children with pathological short stature were significantly smaller and deviated more from target height. A significant proportion of the children with pathology had height SDS above the referral threshold, suggesting the UK cut-off may be too strict. Routine assessment of target height deficit could improve the sensitivity for identifying pathological short stature and prevent unnecessary referrals.

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OC5.2

Evaluation of the discrepancy between free thyroxine (FT4) reference ranges and the impact on clinical investigation of central hypothyroidism

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Introduction
Free thyroxine (FT4) assays are available on different commercial platforms where manufacturers provide different reference ranges. The lower limit of normal varies considerably between 8 and 13.9 pmol/l depending on the FT4 assay being used. There is concern about the validity of these reference ranges in paediatric populations, especially for the Roche FT4 assay; here there is a tendency for FT4 results to be below age-related lower limits of 13.9 or 13.6 pmol/l. As a result, children with low FT4 levels with a normal TSH are at risk of being over- or under-investigated for 'central' hypothyroidism.
Methods
Roche Elecsys cobas and Abbott Architect FT4 immunoassays were used. Serum samples ($n = 59$) collected from paediatric patients found to have a normal TSH with a FT4 below the lower limit of normal on the Roche FT4 assay were analysed for FT4 using the Abbott assay (lower limit = 9 pmol/l). Medians were compared using Wilcoxon signed-rank test. A comparison of FT4 results using the two lower limits of normal for each assay was performed.
Results
The age range of the paediatric patients was from 9 months to 17 years (median age = 14 years). Whilst the median FT4 concentrations were statistically different ($P < 0.001$), they were clinically comparable with FT4 levels of 12.5 pmol/l and 11 pmol/l for the Roche and Abbott assays respectively. All 59 samples were found to have a FT4 within the reference range ($\geq$9 pmol/l) for the Abbott assay.
Conclusions
Hypothyroxinaemia without a raised TSH can result from a number of disorders but most important to exclude is central hypothyroidism which may result from a lesion near the pituitary or hypothalamus. The decision to investigate is critically dependent on the FT4 results. We have shown that with two commonly used assays there is only a small variation in actual FT4 concentrations, but a major difference in manufacturers' reference ranges. All patients in this cohort have euthyroid results with one assay (Abbott) and abnormal results with the other (Roche). This is an unsatisfactory situation and requires resolution.

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OC5.3

An investigation of androgen-responsive non-coding RNAs in boys with atypical genitalia without genetic variants in the androgen receptor (AR)

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Introduction
Transcriptome analysis of peripheral blood mononuclear cells (PBMC) RNA has identified a set of androgen-responsive non-coding RNAs.
Aim
To quantify the androgen-responsive gene expression and investigate its relationship to the testosterone (T) rise following hCG stimulation in boys with no genetic evidence of androgen insensitivity.
Methods
Boys with suspected DSD who were evaluated at the Royal Hospital for Children, Glasgow from 2018 to 2021 were included. Information on clinical, biochemical and genetic assessment was obtained from clinical records. PBMC RNA was collected before and after hCG stimulation of the testes on day 4 (D4) and day 22 (D22) and gene expression was quantified using QuantStudioTM 3D Digital PCR.
Results
Ten XY boys with atypical genitalia, a median age of 0.8 yrs (0.5,3.4) and no detected AR gene variants were included. The median baseline and peak T was 0.5 nmol/l (0.5,6.8) and 21.7 nmol/l (1.2,42.1), respectively. Within this group, there was one patient who did not show a T response to hCG at all on D4 and a minimal response on D22 (1.2 nmol/l). The median fold change in SNORD5 and RNY5 on D4 in this patient was 0.09 and 0.05, respectively. The median fold change for the two genes on D22 was 0.14 and 0.04, respectively. In the rest of the cohort, the median post-hCG T on D4 and D22 was 16 nmol/l (2.5,42) and 25 nmol/l (17,37), respectively. In this group, the median fold change in SNORD5 expression on D4 and D22 was 4.0 (0.25,14) and 1.2 (0.1,5.6), respectively. The median fold change in RNY5 expression on D4 and D22 was 1.0 (0.1,38) and 0.5 (0.2,7.7), respectively.

Conclusions
Expression levels of RNY5 and SNORD5 can be quantified accurately and show androgen dependency. Further research in genetically confirmed cases of androgen insensitivity plus those with no response to hCG stimulation is required to determine the diagnostic role of non-coding RNAs in XY DSD.

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OC5.4

Virtual exercise sessions: An innovative way of promoting physical activity in children and young people with obesity

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The rising prevalence of childhood obesity is a major public health concern. Approximately 21% of children by the age of eleven are clinically obese, with a further 14% classed as overweight. The causes of obesity of childhood obesity are multifaceted, leading to a complex multi-disciplinary management approach. A high proportion of children and young people do not meet the recommended guidelines of a minimum of 60 minutes physical activity per day. In addition to the barrier's families face when accessing sport, the COVID-19 pandemic has caused unprecedented limitations on physical activity levels due to social distancing guidelines and facility closures. Patients with obesity have been greatly impacted as their clinical management involves physical exercise participation. Digital solutions have readily adapted throughout the pandemic to address gaps in patient care, enabling virtual interactions to continue between patients and clinicians. To overcome restrictions, a Tier 3 weight management service delivered virtual exercise sessions to children and young people with obesity. The 30-minute sessions were delivered twice weekly and comprised of a variety of physical activities ranging from circuit style exercises to yoga and meditation. Patients' perceptions to virtual real time sessions have not previously been explored in this cohort of children. To enhance future paediatric weight management services, the perceptions of children with obesity are needed. Semi-structured telephone interviews were conducted on 6 patients from the service who had participated in the sessions, for a duration of six months. The data was transcribed verbatim, reviewed by two independent researchers, and underwent thematic analysis. This study was carried out to establish whether virtual sessions are an acceptable method to improve the activity levels among children and young people with obesity. The respondents favoured virtual exercise over traditional face to face exercise and perceived improvements in both their energy and activity levels, along with an improvement of sleeping routine. The children were consistently motivated to join the virtual exercise sessions due to increased enjoyment and improved confidence upon participation. Our study revealed that virtual sessions enable children and young people with obesity to receive necessary interventions to promote physical activity participation and engagement.

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OC5.5

B-cell class switching in trans- and cis-gendered healthy young people is differentially influenced by sex hormones

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Cis-gender females are known to mount stronger humoral immune responses than cis-gender males. Little is known about the immunophenotypes of transgender individuals on gender-affirming hormonal treatment, despite growing evidence that hormones influence the immune system.Via the process of class-switch recombination (CSR), B-cell immunoglobulin isotype 'switches' from early IgM/IgD classes to IgG/IgA/IgE. Whilst important in infection/vaccine responses; switched isotypes play a significant role in autoimmunity. T-follicular helper cells (Tfh) aid B-cells in CSR. This study investigates the impact of sex-chromosomal complement and hormonal milieu on B-cell CSR, using samples from healthy cis- and trans-gendered individuals to create an *in vivo*, age-adjusted model of these effects. Peripheral blood samples were collected with informed consent from cis-gender male ($n = 35$) and female ($n = 53$) post-pubertal volunteers (14-28y), and trans-gender male (on testosterone and/or GnRH-analogue; $n = 25$) and female (on oestradiol and/or GnRHa; $n = 19$) volunteers (16-19y). In-depth phenotyping of peripheral blood mononuclear cells was performed using multiparameter flow cytometry. GraphPad Prism was used for statistical testing appropriate to the data distribution/number of groups (unpaired t-test/Mann-Whitney U, one-way ANOVA/Kruskal-Wallis). Cis-females had greater percentages of class-switched B-cells than cis-males. In trans-males, GnRHa monotreatment was sufficient to also significantly decrease the levels of class-switched B-cells, and additional testosterone treatment saw no further decrease. GnRHa treatment, with or without oestradiol in trans-females, however, was not associated with the increase seen in cis-females. Indeed, trans-females had the lowest percentages of class-switched B-cells of all groups. Cis-females and -males had similar levels of Tfh cells. Both trans-females and trans-males however, trended toward lower levels of Tfh cells, with little distinction between GnRHa-only and gender-affirming hormones. Sex hormones may differentially affect humoral immune responses of those assigned female at birth vs those assigned male. Whilst trans-males followed the same decreased class-switching pattern as cis-males, a surprising and significant decrease was seen in trans-females, that did not mirror the immune phenotype of cis-females. These data support the need for further research into the interactions between hormones and chromosomal sex, as immunological outcomes in trans-gender people may differ from those in cis-gendered individuals.

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Oral Communications 6

OC6.1

Novel dominant negative GH receptor variants provide important insights into GH receptor physiology

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Background
Growth hormone insensitivity (GHI) is a continuum defined by normal/elevated growth hormone (GH), low IGF-I levels and growth restriction. Non-classical/mild-moderate GHI is poorly characterised and is frequently under-diagnosed. Heterozygous dominant negative (DN) gene variants located in the regions encoding the intracellular/transmembrane domains of the GH receptor cause a 'non-classical' GHI phenotype.
Hypothesis/Objective
Detailed characterisation of novel, naturally occurring dominant negative *GHR* gene variants will improve our understanding of the physiology of human growth and enhance patient care.
Methods
Two novel heterozygous *GHR* variants (c.876-15T>G; MUT 1 and c.902T>G; MUT 2 in intron 8/exon 9, respectively) were identified in 2 GHI patients by our short stature whole genome panel. *In vitro* splicing assays were performed using an exon trap vector. Gibson assembly created *GHR* wild type (WT) and variant (MUT 1 & 2) constructs as well as constructs with either NanoLuc® Large BiT (LgBiT) or Small BiT (SmBiT) subunits. These constructs were transfected into HEK293T cells and western blotting (WB) was performed using anti-STAT5b, anti-pSTAT5, anti-GHBP and anti-NanoLuc® Luciferase antibodies (anti-beta-actin/GAPDH as controls). NanoBiT complementation assays allowed quantitative assessment of WT and MUT GHR homo/hetero dimerization.
Results
In-vitro splicing assays confirmed both *GHR* variants activate the same alternative splice acceptor site resulting in abnormal splicing and exclusion of 26 base pairs of *GHR* exon 9. Wildtype (WT) and MUT constructs were co-transfected to mimic the heterozygous state of patients. WB analysis confirmed the production of truncated MUT variants and reduced GH-induced STAT5B phosphorylation. Analysis of the conditioned cell media demonstrated increased GH binding protein (GHBP) production. Novel NanoBiT complementation assays showed increased luminescence readings of MUT:MUT and WT:MUT GHR homo/heterodimers compared to WT:WT homodimers suggesting increased cell surface expression with MUT GHR receptor homo/heterodimers.
Conclusion
The novel truncated *GHR* variants exert a dominant negative effect with blunted GHR signalling. Increased cell surface expression and GHBP production may also contribute to reduced function of these *GHR* variants. The creation of NanoLuc®-*GHR* constructs provide an innovative methodology for characterising the functional role of *GHR* variants in GH binding and GHBP physiology.

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OC6.2

Body composition in adults with genetically-confirmed Silver-Russell syndrome.

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Silver-Russell syndrome (SRS) is characterised by low birth weight, short stature, and feeding difficulties in childhood, with marked leanness also described. There is limited information on body composition in older people with SRS.
Objective
To evaluate body composition in adults with SRS.
Methods
Participants aged $\geq$18 years with molecularly-confirmed SRS attended a single study appointment. Body composition was evaluated using anthropometry and dual-energy x-ray absorptiometry (DXA) (Hologic Horizon W instrument, Hologic Inc, USA) and the SRS group was compared with men and women aged 19 to 63 years in the Southampton Women's Survey, who are broadly representative of the general population. Continuous variables were compared using the Mann-Whitney U test or independent samples t-test as appropriate. The Chi-squared test was used to compare categorical variables.
Results
25 (13 females) with a median age of 32.9 years (range 22.0-69.7). Loss of methylation at H19/IGF2 was diagnosed in 88%; maternal uniparental disomy for chromosome 7 in 12%. 60% had previously received GH. DXA scanning was performed in 19 participants. Individuals with SRS had a median height SDS of -3.13 (IQR -3.83 to -1.31); median weight SDS -1.83 (IQR -3.76 to -0.11); median BMI SDS -0.47 (IQR -1.83 to 1.53). Median waist-to-hip ratios in women and men were 0.826 and 0.932 respectively. Waist circumferences $\geq$80 cm in women and $\geq$94 cm in men were present in 36%. DXA results showed the following: trunk-to-limb fat was greater in SRS than unaffected individuals (medians 1.21 and 1.02 respectively, $P = 0.03$). Lean mass percentage (median 51.8% vs 66.2%) and lean mass index (mean 13.7 kg/m^2 vs17.3 kg/m^2) were lower in SRS than unaffected individuals (both $P < 0.001$). Fat percentage was greater in SRS than unaffected individuals (44.45% vs 30.32%, $P < 0.001$).
Conclusions
Adults with SRS have lower lean mass, higher body fat percentage and greater central adiposity than unaffected adults. Large cohort studies suggest that this body composition profile is associated with increased cardio-metabolic risk in adulthood. Therefore, childhood management of SRS should aim to mitigate this potential risk in adulthood.

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OC6.3

Topiramate as a treatment option in managing obesity complicated by idiopathic intracranial hypertension and chronic migraine in children and adolescents

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Background
Childhood obesity is associated with multitude of co-morbidities. Idiopathic intracranial hypertension (IIH) is one of the less common co-morbidities in children and young people. Severe migraine has been postulated as a further association. We report our experience of using topiramate for managing obesity associated IIH and severe persistent migraine.
Cases: Case One
A 12 year old boy was referred with morbid obesity, systemic hypertension and IIH. Acetazolamide was used to treat IIH initially but was stopped due to sustained reduction in plasma bicarbonate. Topiramate was commenced, subsequently his weight reduced 4 kg over two months, with a BMI (SDS) improvement from 39.25 (+3.6SDS) to 36.17 (+3.3SDS), a reduction of -0.3 SDS.
Case Two
A 10 year old girl was diagnosed with morbid obesity and associated IIH. Due to progressive weight gain her acetazolamide was switched to topiramate with the aim of achieving weight loss in addition to IIH symptom management. Her weight reduced by of 5.7 kg over ten months, BMI SDS reduced from +1.79 SDS to +0.9 SDS (-0.89 SDS reduction). Her topiramate was stopped two months later as she had attained a normal weight and headaches resolved.
Case Three
A 16 year old girl with persistent migraines was gaining weight despite lifestyle and dietary modifications (IIH had been excluded). She had gained 31.7 kg over two years, her BMI increasing from 37.3 to 44.6 (+3.9 SDS). Sumatriptan and propranolol had provided no benefit to migraines. Topiramate was commenced and her weight reduced by 10.3 kg over five months, her BMI(SDS) reduced from 44.6 (+3.9SDS) to 42.5 (+3.7SDS), a reduction of -0.2 SDS. The median BMI SDS reduction was -0.3 SDS in the above patients along with sustained improvement of their clinical symptoms in a short time span. None of the patients experienced significant side effects from topiramate.
Discussion
Topiramate is known to suppress appetite but whether mainly through appetite suppression and consequent weight loss or by carbonic anhydrase inhibition is not fully determined. Topiramate could be considered as potential therapy in IIH or severe persistent migraine associated with obesity. Randomised trials on topiramate involving children and adolescents would be beneficial.

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OC6.4

Final height SDS of paediatric patients with ESRF that underwent renal transplantation

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Objective
Impaired linear growth is a common complication of end stage renal failure (ESRF), with recombinant human growth hormone (rhGH) being the suggested treatment until renal transplantation (RTx). Growth improvement post RTx has been reported, however data on the degree of catch up growth post RTx and final height (FH) is limited. We aimed to evaluate the effect of RTx on FH standard deviation score (SDS) and the possible contributing factors.
Methods
We performed a retrospective review of medical records of RTx recipients from a single UK centre. We recorded demographic data, height SDS before RTx and FH SDS, treatment with rhGH and eGFR until FH. We analyzed change in height SDS prior to RTx and at FH and possible predictive factors.
Results
33 RTx patients (17 males/16 females) with normal graft function were included. Mean age of RTx was 9.5 years. RhGH was administered before RTx in 12 patients. Height SDS increased significantly from pre RTx (mean Ht SDS -2.0, median -2.0, range -4.33 to 1.88) to FH (mean Ht SDS -0.9, median -1.13, range -3.72 to 1.37), $P < 0.001$. 29 patients (88%) had a normal height > -2.0 SD. The mean change on height SDS from before RTx to FH was +1.1. There was a significant correlation between age of RTx and increase of height SDS from before RTx to FH, R: -0.373, $P = 0.032$. Multiple regression analysis (including age of RTx, rhGH treatment before RTx and gender) showed that age of RTx was an independent predictive factor of the height SDS increase.
Conclusion
In our group, we observed a sustained increase in height post RTx resulting in normal FH. RTx especially in younger recipients seems to result in adequate catch up growth that can compensate for the deficit occurring due to ESRF.

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OC6.5

Highlighting POLE1 mutations as a cause of adrenal insufficiency

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Background
Compound heterozygous POLE1 mutations have previously been described as a cause of IMAGe syndrome. The severity of the adrenal insufficiency (AI) at initial presentation has been a subject of ongoing debate.
Case report
At 22 weeks gestation the proband's mother was referred to paediatric endocrinology for low oestriol on antenatal quadruple testing. The pregnancy was complicated by severe growth restriction leading to emergency caesarean section at 34 weeks. The baby weighed 1.3 kg and was admitted to NICU with respiratory distress, hypoglycemia and jaundice. Synacthen testing on day 4 confirmed primary AI. Cortisol concentrations were 149nmol/l at 0 minutes and 152 nmol/l at 30 minutes, with baseline ACTH of 1250ng/l. USP demonstrated low concentrations of all cortisol metabolites. Ultrasound and MRI abdomen did not visualise the adrenals. USS hips showed bilateral dysplastic hips. Karyotype was XX. No abnormalities were identified on adrenal gene panel (AAAS, AIRE, CDKN1C, CYP11A1, MC2R, MRAP, NNT, NR0B1, NR5A1, SAMD9, SGPL1, STAR, TBX19). Targeted trio exome sequencing identified the presence of compound heterozygous POLE1 pathogenic variants; a frameshift variant c.4260_4261insACAG and a recurrent splicing variant, c.1686+32C>G. The patient is currently on adrenal replacement therapy (hydrocortisone and fludrocortisone) and sodium chloride supplements. She continues to require NGT feeds; height and weight remain -4SD. Initial immune workup demonstrates low immunoglobulins and T cell concentrations.
Discussion
This case report demonstrates the importance of early investigation for AI in babies born to mothers with low oestriol on antenatal quadruple testing. It highlights that current adrenal panels do not include all genes associated with AI. Making a rapid diagnosis in this infant led to early assessment of immune function and enabled discharge home as extreme growth failure is an expected finding in IMAGe.

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Oral Communications 7

OC7.1

Utility of glycated haemoglobin in assessing abnormal glucose homeostasis in children and adolescents with obesity undergoing oral glucose tolerance test

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Background
Childhood obesity and type 2 diabetes mellitus (T2DM) have increased proportionately in the last decade. Oral glucose tolerance test (OGTT) is recommended for paediatric patients with a BMI >98th centile (NICE, 2014) to identify T2DM or abnormal glucose homeostasis (AGH).
Aim
To estimate the proportion of patients with AGH/T2DM seen in a tier 3 obesity service and evaluate the utility of the glycated haemoglobin (HbA1C) in detecting AGH.
Methods
Retrospective data were collected from children and young people (CYP) with obesity undergoing an OGTT between 2015-2020. Fasting blood glucose (FBG), 2 h post-prandial glucose (PPG), fasting insulin and HbA1C were recorded. Any clinical features of insulin resistance were documented. OGTT results were interpreted using WHO (2006) criteria.
Results
Of 113 CYP (mean age 13.2 years), 52 were male and mean body mass index (BMI) was 32.1 kg/m2 (+2.77SDS). 6 patients (5.3%, 5 Caucasian, 1 Black African ethnicity) were diagnosed with T2DM. 5 (4.5%) had impaired glucose tolerance (IGT) (2-hour PPG 7.8-11 mmol/l) and 1 (1%) had both impaired fasting glycaemia (IFG) (FBG 6.1-6.9 mmol/l) and IGT. 101 patients (90%) had a normal OGTT. Median HbA1C at diagnosis was 53.5 mmol/mol (49-94) for those with T2DM and 40 mmol/mol (33-45 mmol/mol) for those with for those with IFG/IGT. HbA1c $\geq$ 48 mmol/l was predictive of T2DM with sensitivity 100% (95% CI 54.1 - 100), specificity 100% (95% CI 96.6 - 100) and positive predictive value (PPV) of 85.7% (95% CI 46.0 -97.7). HbA1c > 43 mmol/mol was predictive of detecting AGH with sensitivity 66.7% (95% CI 34 - 90), and specificity 97.0% (95% CI 93.03 - 99.76). In patients with normal OGTT average HbA1C was 37 mmol/mol (range = 29-44 mmol/mol). HbA1c $\leq$39 was predictive of normal OGTT with sensitivity 85.3% (95% CI 76.5 – 91.7) and specificity 83.3% (95% CI 58.6 – 96.4).The number-needed-to-screen for one patient to be diagnosed with T2DM or AGH was 28 and 10 respectively.
Conclusion
HbA1C could be considered as a screening tool in CYP with obesity to indicate the requirement for OGTT to detect AGH, potentially avoiding the clinical and cost burden of an invasive test.

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OC7.2

Multi-centre service evaluation of presentation of newly diagnosed type 1 diabetes in children in the U.K. furing the COVID-19 pandemic

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Background
The COVID-19 pandemic led to major changes in the pattern of presentation to Emergency Departments. This prompted concern within Paediatrics that this altered behaviour could lead to delays in the diagnosis of life-threatening conditions such as type 1 diabetes. A multicentre study was conducted to determine the incidence, referral patterns and severity of disease at presentation of this condition.
Methods
This was a U.K.-based multi-centre quality improvement project. It involved paediatric patients with a new diagnosis of type 1 diabetes who attended four treatment centres between 1st January - 31st July 2019 and the corresponding period in 2020. Assessments were made of presentations of the condition pre- (Jan-Mar) and post- (Apr-Jul) lockdown in 2020. A standard proforma was used to collect demographic and clinical data. This allowed total diagnostic interval (T.D.I) and patient interval (P.I.) to be calculated.
Results
Fewer new cases of type 1 diabetes were diagnosed post-lockdown compared with the identical period in 2019 in three of the four units studied. The median T.D.I. and P.I. were significantly lower during the period of lockdown than in the preceding three months of 2020 (P value = 0.039 and P = 0.025) respectively. There was no significant difference in the proportion of patients presenting with diabetic ketoacidosis (DKA), nor in the requirement for PICU admission or for ventilatory support. Patients were more likely to present with severe DKA post-lockdown compared with the other time periods. This difference was not however statistically significant. There was also evidence of change having occurred in the route to diagnosis for children with diabetes post-lockdown in that they were more likely to have presented via the Emergency Department.
Conclusions
The study demonstrated that there was no impairment of systems' ability to make the diagnosis of type 1 diabetes in children the U.K. during the initial phase of the national public health response to the COVID-19 pandemic in 2020. It fully validated the narrative of the RCPCH and others in urging parents/caregivers to continue to promptly access medical services for their children. This provided an immensely positive message at a time of great public uncertainty.

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OC7.3

Hybrid closed-loop in children and young people with type 1 diabetes improves glycaemic management and quality of life measures

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Introduction
Hybrid closed-loop (HCL) systems are characterised by integrating continuous glucose monitoring (CGM) with insulin pumps which automate insulin delivery via specific algorithms and user-initiated insulin delivery.
Objectives
The aim of the study was to evaluate effectiveness of HCLs on HbA1c, time-in-range (TIR), hypoglycaemia frequency and quality of life measures in children and young people (CYP) with T1D, and their carers.
Methods
CYP with T1D on HCL were included in the study. Data on HbA1c, TIR and hypoglycaemia frequency was reviewed 3 months prior to starting the HCL and 3 months after. As part of clinical care, all patients and carers were provided with key education on the use of the HCL system by trained diabetes healthcare professionals. All patients and carers also completed the specific mandatory training for the relevant HCL system offered by the industry. CYP aged 12 years and above independently completed the validated Hypoglycaemia Fear Survey (HFS). Parents of patients <12 were asked to complete a modified version of the HFS-Parent survey. A structured questionnaire to assess the quality of life (QOL) impact was also used.
Results
There were 39 CYP (22 males) with T1D included with a mean age of 11.8 $\pm$ 4.4 SD (range 2.6-18.0) at commencement of HCL. Mean duration of diabetes was 3.8 years $\pm$ 2.8 SD. There were 55% of patients who were prepubertal. 91% were on the Tandem Control-IQ system and 9% on the CamAPS FX system. HCL use demonstrated significant improvements at 3 months prior compared to 3 months after commencement in the following: HbA1c (63.0 vs 56.6, $P = 0.03$), TIR (50.5 vs 67.0, $P = 0.001$) and frequency of hypoglycaemia (4.3% vs 2.8%, $P = 0.004$). HFS scores showed improved behaviour (34.0 vs 27.5.9, $P = 0.02$), worry (40.2 vs 31.6, $P = 0.03$) and HFS-P scores also showed improved behaviour ($P < 0.001$) and worry ($P = 0.01$). 76% of carers strongly agreed or agreed they slept better, 97% felt that the diabetes management had improved and 95% felt they had a better quality of life with the HCL.
Conclusion
Our study shows that HCL at 3 months improves glucose control, diabetes management and quality of life measures for patients and carers.

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OC7.4

Patient experiences of the changes made to the Cardiff and Vale University Health Board Paediatric Diabetes service due to COVID-19

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Background
Children and Young People (CYP) with diabetes are encouraged to attend four clinics each year.(1,2) During the COVID-19 pandemic, concerns regarding risk of virus transmission, reduced staff numbers and social distancing requirements, meant the Cardiff and Vale University Health Board (CAVUHB) paediatric diabetes service had to find alternative ways to communicate with patients. This included video consultations and drive-through HbA1c clinics as a substitute for some face-to-face clinics.
Objectives
The aim of this study was to establish children's and young people's and their carer's opinions of the changes made to the CAVUHB paediatric diabetes service during COVID-19 and determine whether they would like video call and drive-through HbA1c clinics to continue after the pandemic.
Methods
This was a quantitative study. Questionnaires were produced and distributed to patients and their carers during the paediatric diabetes clinics held at CAVUHB between 30th March 2021 and 22nd April 2021. The questionnaires were also uploaded to the DigiBete platform and local online parent support groups. This study used non-probability sampling methods.
Results
There were 54 responses to the questionnaire. Face-to-face clinics were rated the most useful, scoring 4.66 out of 5 on average for usefulness and virtual video call clinics were rated 3.75 out of 5. Drive-through HbA1c clinics scored an average of 4.62 out of 5. 46% of participants wanted virtual clinics to continue after COVID-19, 37% only wanted face-to-face clinics and 17% had no preference.
Conclusion
Nearly half of the patients in this service wanted virtual clinics to continue after the pandemic, therefore this is something which the CAVUHB and other paediatric diabetes services may want to consider implementing as a permanent change. All service users could be given a choice in the future of having a virtual video call and drive-through HbA1c appointment as a replacement for some of their face-to-face clinics each year. More research could be done to establish how virtual clinics can be improved to improve patient experience.

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OC7.5

Screening for eating disorders in young people with type 1 diabetes

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Background
Eating disorders (ED) are more prevalent in young people with Type 1 diabetes than their peers and the combination is associated with higher levels of mortality. However, ED are often under-identified in paediatric diabetes services. Using quality improvement methodology, a screening pathway for ED was developed.
Methods
Questionnaires and semi-structured interviews explored participants' views regarding a screening pathway and choice of screening tool. Three validated screening questionnaires were selected for review: DEPS-R, SEEDS and mSCOFF. 108 patients aged 12-18y and their families were invited to participate. 21 healthcare professionals including doctors, nurses, dieticians, psychologists, eating disorders specialists and school staff were also invited to take part. External organisations supporting young people with diabetes or ED were approached as well.
Results
17 young people (12-17y, 62.5% female, 37.5% male), 16 parent/carers and six professionals took part. The paediatric diabetes team were enthusiastic about instituting a formal screening process for ED. Barriers to effective screening were identified as: a lack of training in ED, time constraints, lack of specific guidance/resources and the sensitive/secretive nature of ED. Strengths identified included MDT cohesiveness, good continuity and strong relationships with patients and families. Both young people and professionals preferred the DEPS-R tool, citing its clearer, more specific questions; parent/carers preferred the SEEDS saying it was less invasive. mSCOFF was the least preferred by all groups. Annual review was identified as the best time to incorporate screening, one-to-one away from parents/carers, by a staff member chosen by the young person. Formal training in ED and identifying an ED champion in the diabetes team, joint clinical meetings and shadowing opportunities were also suggested. Teaching sessions on eating disorders in Type 1 diabetes were then delivered to the Paediatric Diabetes team and to the ED team about Type 1 diabetes.
Conclusions and Recommendations
There is a clear need to screen for eating disorders amongst young people with Type 1 diabetes, and to equip staff with knowledge and skills to identify patients at risk. Our service has introduced a formal pathway as part of the annual review process, given specific training to the paediatric diabetes team, and formed a closer partnership with ED services.

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Oral Communications 8

OC8.1

Cystic fibrosis related diabetes (CFRD): could Cystic Fibrosis Transport Receptor (CFTR) modulators be the answer?

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Background
Cystic Fibrosis related diabetes affects 40-50% of adults with cystic fibrosis (CF). This can significantly affect pulmonary function and life expectancy. Kaftrio (Ivakaftor, tezacaftor and elexacaftor) has recently been licensed for use in CF. Previous data highlight that glucose regulation may be altered on commencing this treatment.
Methods
Eight children and young people (CYP), aged 14 (12-15) years, who were diagnosed with CFRD aged 12.8 (8.7-13.2) years, commenced Kaftrio. Freestyle Libre monitoring was commenced 2-5 days prior to starting treatment and

continued for 7 days after. This was repeated at six monthly intervals, or earlier if clinically indicated. Insulin doses were reduced or stopped on commencing Kaftrio. Data were available for six CYP.
Results
Of the two children with no Libre data available, one stopped insulin and the other remains on long and short acting insulin at significant doses.
Discussion
Our data show that glucose regulation is affected in children with CFRD when they are commenced on Kaftrio. Insulin may no longer be required. Alternatively, insulin doses may reduce significantly. Monitoring for hypoglycaemia and education are required, even for those no longer requiring insulin. CYP may need to re-introduce insulin at smaller doses over the following year. Further data on long term effects need to be assessed.

Table 1 Libre data and insulin doses pre-Kaftrio, immediately post Kaftrio and 5-13 months after starting Kaftrio.

	Pre-kaftrio (median, [range])	Immediately post Kaftrio (median, [range])	5-13 months post Kaftrio (median, [range])
Time period monitored (days)	6.0 [2.0-7.0]	7.0 [7.0-7.0]	10.5 [7.0-14.0]
Time sensor active (%)	69.5 [27.0-98.0]	90.5 [62.0-100.0]	54.0 [6.0-73.0]
Average glucose (mmol/l)	6.3 [5.9-7.5]	6.0 [5.7-7.4]	6.5 [5.3-7.0]
Glucose variability	27.7 [21.0-39.0]	25.1 [18.1-39.9]	26.3 [18.6-37.1]
% time glucose within target range (%)	95.0 [73.0-98.0]	94.5 [70.0-99.0]	93.5 [88.0-99.00]
% time glucose >10 mmol/l (%)	5.0 [0.0-21.0]	2.0 [0.0-23.0]	3.0 [0-16.0]
% time glucose <3 mmol/l (%)	1.5 [0.0-6.0]	6.0 [0.0-7.0]	2.0 [0.0-12.0]
Number of hypoglycaemic episodes recorded	1.0 [0.0-1.0]	0.5 [1.0-6.0]	1.5 [0.0-17.0]
Dose of insulin (units/day)	7.0 (2.0-25.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)

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OC8.2

The cost of diabetes school training was halved whilst training 25% more staff during COVID-19 using multi-media interactive care plans

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Introduction
The COVID-19 pandemic prevented face-to-face school diabetes training in 2020/2021 at Birmingham Women's and Children's Hospital. Moving school training online was the only viable option to ensure children with type 1 diabetes could attend school.
Objectives
1. Develop an online school training package with competency assessment for all diabetes devices 2. Audit the number of staff competent and the cost and acceptability of the training package.
Methodology
Step 1: Over fifty multi-media interactive PDF care plans covering all devices were created, allowing personalisation upon entering age, weight and preferred hypo treatment using JavaScript coding. Each care plan had at least ten short videos embedded summarising the teaching. Each care plan had a google form competency questionnaire allowing self-assessment where 80% was the minimum pass mark Step 2: The new care plans were populated and sent to the schools with email instructions. Step 3: Compare the number of competent school staff and service cost of face-to-face training from September 2019 to March 2020 (F2F) vs online training from September 2020 to March 2021 (ONLINE). Also, the acceptability of online training.
Results
Total number of school staff trained and competent for F2F was 300 vs 375 for ONLINE, a 25% increase. Total service cost (health care professional time, room hire, material generation, admin, telephone queries) for F2F was £10,050 vs £4,290 for ONLINE, a 58% cost reduction. The principal saving was 190 fewer hours of nurse/dietitian time (£20 per hour) required to train school staff, a £3,800 saving. Qualitative feedback from school staff showed 1) training time remained at two and half hours, but travel time reduced by over an hour 2) videos enabled self-paced learning and re-visiting essential teaching at the time of need 3) no limits on staff to be trained 4) Competency assessment provided re-assurance.
Conclusion
Moving school training online reduced the service cost by over half whilst training 25% more school staff. Multi-media interactive school care plans allow self-paced learning and re-visiting videos at the time of need. Birmingham Women's and Children's Hospital Diabetes Team plan to keep school training online.

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OC8.3

Nottingham's Robin Hood approach to socioeconomic and ethnic disparities in paediatric diabetes

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Introduction
Racism is a fundamental determinant of health, described by Prof Kevin Fenton (PHE) as a "wicked problem"- a complex problem highly resistant to solutions. The amplification of the voice of black lives matter" and disproportionate number of deaths from Covid-19 in Black and Asian people has re-focussed attention on racial health inequalities. Structural racism and unconscious bias is present throughout medicine. The National Paediatric Diabetes Audit (NPDA) continues to reveal widening socioeconomic and ethnic disparities concerning use of technologies associated with lower HbA1c, and improved health outcomes. Nationally, use of insulin pump therapy is almost twice as likely in White British children (39.8%) compared to Black children (26.7%) and yearly mean HbA1c remains higher in Black children independent of deprivation.
Methods
Using data from the diamond database and NPDA, we measured insulin pump usage, HbA1c, age, ethnicity, and socioeconomic quintile, in the 387 children with type one diabetes in Nottingham from April 2020 to March 2021. In line with the NPDA we excluded HbA1c results taken within 90 days of diagnosis.
Results
Nottingham has a higher proportion of children in the most deprived quintile (30.4%) compared to national average (23.9%)[2], and higher pump usage 52.4% (38% nationally). The national trend of pump distribution and HbA1c is reversed; the least deprived receive the fewest pumps (41%) and have the highest HbA1c (63 mmol/l), and the most deprived use most pumps (63%) with lower HbA1c (57 mmol/l). There is more equitable pump use across all ethnic groups compared to nationally (in brackets), White: 54% (40%), Asian: 56% (30%), Mixed 46%, (35%), and Black 41% (27%) but children of "other ethnic origin" are the least likely to receive pump therapy 0% (35%), however numbers are low ($n = 14$). Mean HbA1c was lower across all ethnic groups than nationally (), with White: 57.1 mmol/l (64.6), Asian: 56.2 mmol/l (65.8), Mixed 63.6 (67.1), and Black: 58.8 mmol/l (71.9).
Conclusion
Nottingham is significantly ahead of the national average for pump provision and HbA1c in Black and Asian children, but must continue to identify and mitigate against barriers to ethnic and socioeconomic equality in order to see excellent outcomes for all.

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OC8.4

Developing a clinical decision aid for paediatric diabetic ketoacidosis: the DKA Calculator

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Diabetic Ketoacidosis (DKA) is a significant complication of paediatric diabetes, the effective management of which relies on meticulous calculations, and timely decision making in response to changing physiology. A previous regional audit in South West England has shown that compliance with national guidelines is highly variable, and errors in calculations such as fluid rates are common. Fluid management in paediatric DKA is a subject of ongoing debate and changing guidance. In addition the multi-step nature of some of these calculations may contribute to this variability in practice. To address this safety concern we developed a clinical decision aid: the 'DKA Calculator'. Clinicians can use this

tool to generate an individualised version of the BSPED Integrated Care Pathway (ICP) for the management of children and young people with DKA, with important variables calculated automatically and pre-filled. These include bolus volumes, fluid and insulin rates, and a suggested timeline for clinical reviews. We hope that providing pre-calculated values for the clinician will add an additional layer of protection against errors, especially when combined with the clear flowchart structure of the ICP. The 'DKA Calculator' is a web application that accepts inputted data such as blood pH, patient weight and the presence of shock. Relevant calculations are performed on the client device using JavaScript. The ICP with these pre-filled values can then be downloaded as a PDF document and printed for use in the patient notes. Data entered into the application (excluding patient identifiable data) is stored in a pseudo-anonymised state for future audit. The programmed logic underwent internal review and is available open-source on GitHub. The 'DKA Calculator' is registered with the MHRA as a medical device in the UK. We describe the development, testing and release of the DKA Calculator, and proposals for future advancements.

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OC8.5

Permanent neonatal diabetes due to KCNJ11 mutation: early successful transition to Glibenclamide and stable glucose profile with multiple daily dosing

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Introduction
Neonatal diabetes (ND) usually presents before 6 months of age and 50% of cases are transient and 50% permanent with more than 20 known genetic causes. Early recognition and urgent genetic testing are important to enable appropriate, precise treatment. Mutations in *KCNJ11* cause ND responsive to glibenclamide, alleviating the need for insulin administration, but there are limited reports of early successful transition.
Case
This infant was born at 37 weeks' gestation weighing 2.07 kg (2nd centile). She had persistent hyperglycaemia (blood glucose >12 mmol/l) requiring intravenous insulin. Her father has diabetes due to a *KCNJ11* mutation managed with glimepiride. The baby was started on glibenclamide early at 10 days of age (0.05 mg/kg/day), following which insulin was stopped. Subsequently, genetic results confirmed paternally inherited missense variant *KCNJ11* p.(Arg201His). Glibenclamide was initially administered as crushed tablets dissolved in water as the only licenced suspension (Amglidia; 0.6 mg/ml) was not readily available and impractical due to small dose requirements. Multiple hypoglycaemias were noted despite reducing the dose to 0.02 mg/kg/day possibly indicating that crushed tablets were causing unreliable dose distribution. Continuous glucose monitoring (CGM) using Dexcom G6 was initiated at 3 weeks of age which also showed multiple hypoglycaemias. Therefore, an in-house suspension was urgently prepared by our local pharmacy at a concentration of 0.2 mg/ml. With this formulation, twice to thrice daily divided doses (0.5 mg/kg/day) were found to cause fluctuations in blood glucose (BG) levels with hypoglycaemia (<3 mmol/l) post-dose and hyperglycaemia (>15 mmol/l) before doses. Increasing the dose frequency to 5-times-daily achieved a stable BG profile without rapid excursions between doses or significant hypoglycaemia. Average BG on CGM improved to 7-8 mmol/l and HbA1c reduced from 58 mmol/mol to 44 mmol/mol. The patient is now 5 months and continues to gain weight (9th centile) with no current developmental concerns.
Discussion
Early commencement of glibenclamide is associated with better neurodevelopmental outcomes in ND. Crushed tablet forms are not ideal in neonates as they may have unreliable dose distribution but limited availability of glibenclamide suspension form may prove challenging. In ND, small frequent doses of suspension may reduce BG variability and enable a more stable profile than twice daily doses.

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OC8.6

Evaluation of the diabetes education app

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Introduction
Structured education is an integral part of type one diabetes care for children and young people and their families, delivered at diagnosis. There is currently no validated curriculum or outcome measures of diabetes education in the UK. We evaluated the outcome of using the diabetes education app (deapp), using flipped learning against historical practice, to determine if it conferred any benefit in our single centre.
Methods
Two cohorts of patients were identified via the diamond database, diagnosed either pre or post deapp. Consenting individuals completed four online questionnaires: the hypoglycaemia awareness (Clarke) questionnaire; fear of hypoglycaemia questionnaire; problems associated in diabetes 20 (PAID-20) questionnaire and; assessment of understanding. Eighteen months of HbA1c data was collected for each patient from diagnosis and length of stay using the hospital database. Staff also completed questionnaires on their experiences of using deapp.
Results
Fifty patients were identified, with 32 consenting to take part ($n = 17$ pre-deapp, $n = 15$ post-deapp). Mean hbA1c over 18 months from diagnosis showed a percentage fall of 52% pre-deapp vs 48% post-deapp (mean hbA1c pre-deapp 109 mmol/l fell to 53 mmol/l vs 101 mmol/l post-deapp fell to 52 mmol/l). Mean clarke scores were 0.3 (pre-deapp) and 1.4 (post-deapp). Mean fear of hypoglycaemia scores were 8 (pre-deapp) and 10 (post-deapp). Mean PAID-20 scores were 16 (pre-deapp) and 22 (post-deapp). Assessment of understanding of diabetes showed a mean score of 35 (60% pre-deapp) and 39 (67% post-deapp). Mean length of stay was 3 days (pre-deapp) and 2 days (post-deapp).
Conclusion
There was equivalent reduction of hba1c to target in both groups. There was no difference in either hypoglycaemia awareness or fear of hypoglycaemia. There were higher PAID-20 scores in the post-deapp group. Staff reported better retention of knowledge and improved engagement in the post-deapp group. There was a reduction in admission time by one day in the deapp group. The findings show equivalence of glycaemic control up to 18 months in the two groups. Deapp appears to reduce bed-stay and demonstrated better knowledge retention as assessed by the two objective measures used. These findings support deapp as a flexible form of education, especially during a pandemic.

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OC8.7

HENRY: High HbA1c service Evaluation 2016-2019: New "tipping point" in contact Required for CYPwD

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Background
Children and young people (CYPwD) with a persistent high HbA1c are at greater risk of developmental and long-term complications. Diabetes services across the England & Wales are mandated to have a 'high HbA1c' policy by the Best Practice Tariff quality standards, to improve health outcomes.
Aim
To evaluate the Birmingham Women's and Children's (BWC) Diabetes Team 'High HbA1c Policy' from 2016 – 2019.
Methods
Data extraction from the Twinkle database. Main outcome measures for the type 1 & 2 diabetes cohort from 2016-19 were; mean HbA1c, percentage of cohort with one or two HbA1c's above different cut-offs from 64 mmol/mol to 86 mmol/mol, and the change in HbA1c for CYPwD attending and not attending the new high HbA1c clinic model implemented in 2018.
Results & discussion
In 2017 there was a 15 mmol/mol ($P < 0.01$) lower HbA1c over the year for those CYPWD with a high HbA1c receiving ten or more face to face contacts, the "tipping point". The "tipping point" was implemented by a new high HbA1c clinic model in 2018, which mandates two, nurse or dietitian appointments between three monthly clinics. The new model resulted in a reduction in overall cohort HbA1c from 67.8 mmol/mol in 2017 to 63.3 mmol/mol in 2018 ($P < 0.01$), making the BWC Diabetes Team a positive outlier for HbA1c in the NPDA national audit. The success of 2018 was driven by two things. Firstly, the purposeful communication of what is a high HbA1c to all CYPWD. Secondly, the CYPwD who attended their high HbA1c clinic appointments reduced their HbA1c by 10.2 mmol/mol ($P < 0.01$). Those who did not attend, mainly those with an HbA1c 86 mmol/mol, increased their HbA1c by 12.2 mmol/mol ($P < 0.01$). The introduction of a clinical administrator in 2019 increased high HbaA1c clinic attendance by 59%, whilst dropping the DNA rate by 50%. This resulted in further HbA1c reductions.

Conclusion
Using purposeful communication to exceed the "tipping point" of annual face to face contact for CYPwD with a high HbA1c appears essential to improve glycaemic control. Dedicated clinical administration staff is vital for clinic efficiency and effectiveness. A new strategy is needed for those with a HbA1c 86 mmol/mol.

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OC8.8

Barriers to uploading diabetes technology at home

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Background
Our department cares for 273 children with type 1 diabetes (T1DM). All T1DM patients are issued with an uploadable glucose meter from diagnosis. 101 patients (37%) use insulin pump therapy and 126 (46%) use a continuous glucose monitoring device. Anecdotally we noted many patients were not uploading their data prior to coming to clinic. This contributed to reduced patient flow through diabetes clinics and also to reduced patient and carer engagement with their diabetes data between clinic appointments. We wanted to better understand the barriers to uploading diabetes devices at home, to enable us to better support this area of self-management.
Method
We conducted a survey of patients attending clinic over a 4 week period between mid April and mid May 2021. We collected information including length of time since diagnosis, devices used, which devices had been uploaded at home and any barriers to uploading. Questionnaires were distributed in clinic and anonymous responses were collected.
Results
We received 36 responses. 44% of patients (16/36) did not upload their diabetes equipment at home prior to clinic. An additional 55% (20/36 patients) were using Dexcom, and so had their data automatically uploaded to Diasend. Barriers to uploading were identified as 'forgetting to upload (22.5%)', not knowing this was expected of patients/families (22.2%), 'assuming clinic staff would do this' (11.1%), not knowing how to (16.7%) or not having access to a computer (11.1%).
Conclusion
A significant number of patients are not currently uploading their data prior to coming to clinic, potentially contributing to longer clinic waiting times and missed learning opportunities. Based on feedback from patients we have instigated a number of changes to our service including changing our clinic appointment letter to highlight to families the importance of uploading devices at home. We have produced a series of leaflets explaining how to upload each separate device, including links to videos. We have approached a local charity to explore whether they can help families who do not have access to computers. Numbers of patients uploading prior to clinic will be re-assessed formally again after these changes have been instigated.

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OC8.9

Virtual sessions 'cook and count' for young people with type 1 diabetes, using PDSA cycles, meeting young peoples wishes

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Background
At the beginning of the first Covid 19 lockdown the team realized the need for an innovative way of having contact with young people. Virtual sessions could do this? We also needed to meet young person's wishes.
Objectives
-For the activity to be fun.
-Improve carbohydrate counting, knowledge, expertise and confidence
-Give young people skills to be independent with their carb counting skills
-Focus on those moving from primary school to secondary schools
-Peer support to reduce isolation of lockdown.
-Using technology young people are familiar with as well as ingredients they are likely to have or easily acquire.
Method
Sessions run by Zoom, virtual cooking and carbohydrate counting. The sessions; scones, pizza, mince pies/strawberry stars. Each session is run virtually by a dietician and a diabetes specialist nurse zooming in separately from their kitchens. Bright invite posters, with food examples are e-mailed to all the young people as well as distributed in clinics both face to face and virtual. Those that show interest have a follow up telephone call from a dietician. Use (Plan, Do, Study, Act) to improve the sessions. Aided by 'Survey Monkey'.
Results
75% enjoyed the session a great deal, 25% a lot. 50% said the session had improved their carb counting a great deal, 25% a lot. 75% said they always carb counted prior to the session 100% very likely, to carb count from now on. Suggestions; 'I think if we could vote for what food we make that would be great for the next session' 'I loved showing my family the creations' 'I enjoyed cooking the food and learning how to carb count'
Conclusion
These sessions are a huge success and through the feedback we are able to gear them to young people's wishes. It is essential when doing non-compulsory education that children's needs are met or the sessions will not happen. PDSA cycles let us adapt sessions to young person's needs in this climate of rapidly shifting challenges. Technology allows us to for-fill the objectives. We hope by using Survey Monkey we can gage it to an older age group too

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Oral Communications 9

OC9.1

Variability in the diagnosis of growth hormone deficiency using dynamic tests. Time for robust pre-test criteria?

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Background
Insulin tolerance test (ITT) is the gold-standard investigation in children with suspected growth hormone deficiency (GHD). Despite their benefits, ITTs are resource intensive, potentially dangerous and can result in unnecessary treatment due to false positive results in children that are at low risk for GHD.
Methods
Retrospective analysis of all paediatric patients undergoing an ITT in two tertiary hospitals in the UK (centre A between 2017-2021, centre B 2016-2019). We determined baseline patient characteristics and proportion of normal tests by centre and patient group (high risk [HR]: pituitary abnormality including oncology patients; low risk [LR]: isolated short stature).
Results and discussion
Proportions of female patients were 28%(A) and 35%(B) ($P = .2$). Patients at centre A were 1.4 years older (mean ages 13.4, 12 years; $P < .01$) and had slightly lower BMI SDS (mean BMI SDS -0.49, -0.09; $P = .047$). Only 3 patients (2 centre A) had BMI SDS > 3. The proportion of HR patients was lower in centre A (16% vs 39%; $P < .001$). Only ITTs where blood glucose < 2.2 mmol/l had been achieved and no growth hormone (GH) values were missing were included ($n = 108$ centre A, $n = 222$ centre B). GH cut off for a normal test was $\geq 6.7\mu g/l$ or $\geq 3\mu g/l$ for patients who had completed growth. In centre A, 58% of ITTs were normal, compared to 39% in centre B ($P = .002$). When only LR patients ($n = 227$) were considered, the difference between centres remained (63% vs 48% normal ITTs, $P = .039$). The difference still stood when ITT results only from young (< 12 years) LR children ($n = 103$) were analysed (61% vs 35% normal ITTs, $P = .03$). Among HR patients ($n = 103$) 35% and 26% of ITTs were normal, respectively ($P = .6$).
Conclusions
When ITTs were performed on low risk patients, centre A had a significantly higher proportion of normal results. This was not explained by baseline patient demographics. Although consensus in diagnostic GH cut-off levels has been reached, variability in clinical practice between centres can explain the observed difference and highlight the importance of using robust pretest clinical criteria especially in children at low risk for GHD.

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OC9.2

Sex steroid priming for growth hormone stimulation testing – a systematic review

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Background
Growth hormone stimulation testing (GHST) is used to diagnose growth hormone deficiency (GHD) in children. Given that sex steroids impact on anterior pituitary function, there is concern around the efficacy of GH stimulation testing in pre/peripubertal children, where sex steroid levels are low. Sex steroid priming prior to GH stimulation testing is thought to improve test efficacy in these children, however evidence to support its use in clinical practice is limited.
Objectives and Rationale
In this systematic review, we addressed the following research questions: Does priming increase GH stimulation test efficacy in pre/peripubertal children? Does priming identify those who would benefit most from treatment in terms of final height?
Search Methods
The study was registered with PROSPERO (registration: CRD42021244443). We searched Medline, Cochrane Library, Scopus, EMBASE and Web of Science and included all studies that included GHST in both primed and unprimed children. A GH cut-off of 7ng/ml was used as a threshold for GHD. Study quality was assessed using the Risk Of Bias In Non-Randomized Studies (ROBINS-I) tool or the revised Cochrane risk-of-bias tool for Randomised trials.
Results
From 127 articles identified in the initial search, 15 studies (954 patients) met our inclusion criteria. This included 4 randomised controlled trials (RCTs). The majority (9/13) of studies indicated that priming increases growth hormone response upon GHST in pre/peri-pubertal children, increasing test specificity. For 3/13 studies (all non-RCTs) the mean GH was <7ng/ml (i.e. GHD) in 'unprimed' patients, compared with >7ng/ml in primed patients. Those treated for GHD based on 'primed' GHST reached a greater final height compared to those with untreated constitutional delay of growth and puberty (CDGP) ($P = 0.023$), whilst for those diagnosed by 'unprimed' GHST, there was no difference compared with untreated CDGP ($P > 0.05$).
Conclusion
Overall, the majority of studies suggest that sex steroid priming increases GH response in pre/peripubertal children, increasing GHST specificity and reducing false positive GHD diagnoses. Further studies are required to determine optimal regimen and specific criteria (e.g. age, pubertal stage) to define those individuals who would benefit from priming.

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OC9.3

Investigating paediatric weight management apps

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Background
Childhood obesity is the single most pressing public health emergency of the 21st century. The prevalence has increased at alarming rates and globally over 41 million children under 5 years of age are classified as overweight/obese. Overweight and obese children are likely to stay obese as adults and develop multi-morbidities including type 2 diabetes, cancer, non-alcoholic fatty liver disease (NAFLD) and cardiovascular disease at an earlier age. The availability of technology has revolutionised the development of applications (apps).
Aim
Many app developers have focused on weight loss and/or calorie counting. This may not be the main aim for children. Our aim was to study the current landscape of obesity apps available on the market for children.
Methods
The search terms 'obesity', 'weight', 'calorie', 'diet', 'obesity children', 'weight management', 'diet apps, 'calorie counter kids', 'weight loss' were used on the Apple Store and Google Play Store. We also searched Google and the NHS app sites.
Results
The top 60 apps from the search were studied and after removing duplicates resulted in 46 apps. Studying 46 apps in detail we found that only 7 of the 46 were appropriate for children under the age of 12 and 4/46 apps approved by a medical body, 3 by the NHS (NHS weight loss plan, MyFitnessPal and Nutracheck) and 1 by the American Academy of Pediatrics Institute for Healthy Childhood Weight (Change Talk). Apps that calculated a child's BMI did not include BMI SDS or z-scores to enable understanding of normal range BMI in the context of age and sex. None of the apps linked in with local services and very few catered for culturally diversity in the context of different languages and cuisines.
Conclusion
There are very few child-friendly obesity apps available that incorporates exercise and diet measurements in a culturally appropriate manner. These would be important considerations in our development of a healthy weight app appropriate for children, young people and their families.

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OC9.4

Changes in trends in Short Synacthen Test use over a decade - a single centre experience

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Background
The Short Synacthen Test (SST) is the most popular test of adrenal insufficiency (AI) worldwide. The current SST protocol at Sheffield Children's Hospital (SCH) recommends measurement of serum cortisol at baseline, then 30- and 60-minutes post stimulation. A peak cortisol of >429nmol/l constitutes a pass. Our practise has evolved to consider results between 350 and 429nmol/l as "borderline" and these patients may be treated with stress dosing steroids only rather than replacement, depending on the clinical scenario. Our group has previously published a study examining the variation in dose following dilution of Synacthen during a low-dose SST (LDSST). We undertook a review of our SST data over a nine-year period.
Methods
We conducted a retrospective analysis of all SSTs performed at SCH from 2011-2019. Numbers of tests performed, Synacthen dose, cortisol results, time of peak cortisol, steroid history and outcome were extracted from laboratory records and electronic patient notes. We used descriptive statistics to summarise the data.
Results
We analysed 1275 SSTs. The number of SSTs being performed at SCH have increased 54%, from 114/yr to 175, but the incidence of AI remained constant (~40 cases/yr). The proportion of tests using the standard dose (SDSST) has increased annually and by 2019 all tests were performed using 145mcg/m^2 dose. Timing of peak cortisol was dependant on SST dose with 58% (214/367) of LDSST peaking at 30mins and 96% (483/501) of SDSST peaking at 60-mins. Only sampling at 60mins during the SDSST would have resulted in a cost saving of £948 in 2019. Peak cortisol results were "borderline" in 122 (9.6%) patients, and this proportion remained consistent over the decade. The management of patients with a borderline result depended on their pre-test probability for AI, cortisol result, and steroid history.
Discussion
Our SST requests, dose and interpretative practice have evolved over the last decade. The number of SSTs conducted each year continues to increase without a change in the incidence of AI. We postulate this is due to increasing concern about steroid induced AI and indicates a need for more effective screening of patients deemed to be at risk.

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OC9.5

Variability of advice and education for steroid sick day dosing in Duchenne Muscular Dystrophy: Results of a UK patient survey

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Introduction

The use of long-term oral corticosteroids in DMD leads to secondary adrenal insufficiency. The 2018 international care consensus recognizes this important issue and recommends emergency plans to be in place.

Aim

This online UK-wide patient survey aims to determine the advice/education given for emergency stress dose plans and the impact of the COVID-19 pandemic in corticosteroid-treated young people with DMD.

Methods

The survey was circulated between November 2020 and January 2021. Results were presented as median (range).

Results

A total of 130 responses were obtained from 129 parents/guardians of a person with DMD. One parent provided responses for twins. Median age of the person with DMD was 11.5 years (5, 26). Eighty-three of 130(64%) were on daily corticosteroids. Sixty of the 130(46%) had access to hydrocortisone for injection. Of those 60, 42/60(70%) had received some form of training. The training involved a practice injection in 34/42(81%). Thirty-four of 42(81%) who received training felt confident about administering an injection as opposed to 9/18(50%) of those who did not receive any training. Forty-one of 42(98%) who received training were clear on when injectable hydrocortisone is needed as opposed to 14/18(78%) of those who did not receive training. Prior to the COVID-19 pandemic [February 2020], 43/130(33%) were provided with an oral emergency stress dose plan for mild-moderate acute illness. After February 2020, the number of patients who were given an oral stress dose plan increased to 66/130(51%). A total of seven oral stress dose plans were identified for those on daily corticosteroid and a greater number of plans in those on the intermittent regimen (during the on and off days).

Conclusion

Despite the known risk of adrenal crisis in patients who are treated with long-term corticosteroid and recent international guidance, emergency sick day plans were not consistently in place in this national survey of boys with DMD. Solutions must take a multi-dimensional and multi-disciplinary approach. Guidance at a national level and the development of structured education for patients and hospital clinicians maybe steps towards improving clinical outcomes.

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OC9.6

'Think Adrenal': An innovative trust-wide safety and education programme designed for the care of patients with adrenal insufficiency

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Over 700 patients with known adrenal insufficiency are treated across the trust. Whilst unwell or fasting for a procedure, these patients potentially risk suffering an adrenal crisis. A flagging system has already been implemented on the electronic patient records (EPR) which identifies patients who are 'on replacement Hydrocortisone'. Following an inpatient adrenal crisis which could have been more optimally managed, we sought to highlight care of this vulnerable cohort across the trust. Additionally, we wanted teams to consider those on long-term steroids who could potentially be at risk of unrecognised adrenal insufficiency whilst unwell. The Endocrine team initiated a trust-wide safety and education project called 'Think Adrenal'. Firstly, we developed interactive patient banners on the EPR for patients with an 'FYI' flag in place. When clicked, a sidebar report opens for all clinical users.

This contains

- Emergency IM dosing regimens
- A 'traffic light' system for nurses, delineating the care of the well (green), deteriorating (amber) and patients in crisis (red)
- Illness Flow Charts for the medical care team to follow when the child is deteriorating, including dosing regimens.
- A 'Think Adrenal' branded bedside 'WETFLAG' which is available for the treatment team to print off, designed alongside the trust resuscitation team.
- Adrenal shift safety checks have been added to EPR to remind nurses to ensure that emergency dosing is prescribed and that the appropriate WETFLAG is in place.

Emergency Hydrocortisone Kits ('grab bags') are now situated on the main wards, ready to be taken with patients when moving around the hospital. In conjunction with these measures, the Endocrine nursing team are leading a trust-wide nurse education drive to empower nurses in the care of these children. This started with training practice educators and has been rolled out to other CNS teams and now onto the wards. Reassuringly, we have already seen incidents in which nurses have correctly suggested potential adrenal crises in a deteriorating child, allowing for subsequent appropriate treatment. The next stage will involve developing education packages for the medical teams in other specialities to be rolled out with the PGME (Post Graduate Medical Education) team.

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Poster Presentations

Adrenal

P1

Analysis of therapy monitoring in the International Congenital Adrenal Hyperplasia Registry

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Background
Congenital Adrenal Hyperplasia (CAH) requires exogenous steroid replacement and can be monitored with 17-OH Progesterone and Androstenedione. We reviewed real world data to evaluate these markers in relation to hydrocortisone dose in patients treated in 21 centres throughout 14 countries.
Method
Retrospective cohort study using pseudonymised data from patients with 21α-Hydroxylase Deficiency recorded in the International Congenital Adrenal Hyperplasia Registry. Assessments between January 2000 and October 2020 in patients prescribed hydrocortisone were reviewed. Recent biomarkers and doses between patients were summarised, and longitudinal assessment of measures within patients was carried out using linear mixed effects models (LMEM).
Results
Recent biomarkers were from a cohort of 345 patients, 52.2% female, median age 4.3 years (Interquartile Range (IQR) 3.1 to 9.2), with median weight z-score of 0.3 (-1.1 to 1.7) taking a median 11.3 mg/m2/day (IQR 8.6 to 14.4) of hydrocortisone. Median 17OH-Progesterone (17OHP) was 35.7nmol/l (IQR 3.0 to 104), 15.9% within a target of 12-36nmol/l and 50.0% above this range. Median Androstenedione (D4) under 12 years was 0nmol/l (IQR 0 to 2)) and those 12 years and over median 10.5nmol/l (IQR 3.9 to 21.0). There were significant differences in biomarkers between centres. Multiple regression showed strongest correlation of D4 with 17OHP when age was a covariate ($P < 0.001$, $R^2 = 0.29$). In Longitudinal assessment, 17OHP did not change with age, whereas D4 increased significantly with age ($D4 = 0.86 + 0.56 \times Age$, $P < 0.001$, $R^2 = 0.08$). Multivariate LMEM showed dose per body surface area (BSA) decreasing by 1.0 mg/m2/day for every 1 point increase in weight z-score. Neither 17OHP nor D4 were statistically significant when added to this model ($P > 0.05$).
Discussion
I-CAH Registry data show large variability in 17OHP and D4, 17OHP commonly above target range and D4 concentrations increasing with age, with significant variability between treatment centres. Hydrocortisone dose per BSA decreases with weight gain and in the absence of poor control, the practice of increasing absolute dose to maintain a specific dose for BSA needs reconsideration.

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P2

Glucose regulation and cardiovascular health in children and young people (CYP) with primary adrenal insufficiency: preliminary data (GRACE study)

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Background
The cardiovascular and metabolic outcomes of patients with AI are poor, and may be related to the non-physiological cortisol profile achieved with hydrocortisone treatment.
Objectives
To describe salivary adrenal biomarkers, glucose and 24 hour ambulatory blood pressure (ABP) profiles, carotid intima media thickness (CIMT) and flow mediated dilatation (FMD) in CYP with primary AI, to improve knowledge of the relationship between non-physiological cortisol exposure, glucose regulation, metabolic and cardiovascular disease. Here we present preliminary data on cardiovascular and glucose parameters.
Methods
CYP, aged 2-18 years were recruited. ABP (24 h, age >10 years only), vascular ultrasound (age >4 years only) and continuous glucose monitoring (CGM) with blinded Dexcom G6 monitor (seven days) were performed.
Results
Twenty-two children (11 male, age 9.1 ± 4.9 years: three Addison's Disease, 19 congenital adrenal hyperplasia,) were recruited. Height was -0.05 ± 1.16SD and BMI +0.77 ± 1.20SD. Hydrocortisone dose was 10.5 ± 3.5 mg/m^2/day. 16 patients (73%) were treated with fludrocortisone, 125 ± 56 micrograms.
CGM data are given in Table 1. One patient did not tolerate CGM.
In six patients (28.6%) glucose was >10 mmol/l for 0.4-2.8% of the time, and in five patients (28.6%) <3 mmol/l for 0.2-2.4% of the time. CIMT ($N = 17$) measured 0.41mm ± 0.04mm (median, IQR), within expected limits. FMD ($N = 15$) measured 8.06 ± 7.9% (median, IQR). FMD was lower than expected for the paediatric population in six patients (11%). ABP was achieved in 11 patients, of whom one was hypertensive.
Conclusion
These preliminary data suggest the glucose profile of CYP with primary AI differs to that of healthy children. FMD may detect early signs of cardiovascular disease, and longitudinal studies are required to ascertain the clinical significance of this observation.

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P3

A cost-benefit analysis of the routine measurement of ACTH as part of the Short Synacthen Test

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Background
Adrenocorticotrophic hormone (ACTH) measurements can help determine the cause of adrenal insufficiency (AI), but AI is diagnosed using peak cortisol levels following Synacthen stimulation, not ACTH levels. ACTH levels are high in primary and low in secondary and tertiary AI. Primary AI is rare in childhood. At

Table 1 Participant and reference data

Parameter	GRACE study (n = 22)	Reference data 6 to <12y (n = 27)	Reference data 12 to <18y (n = 30)
Mean glucose (1SD)	6.13 (±0.64)	5.50 (±0.39)	5.40 (±0.39)
Standard deviation of measurements	1.00 (±0.43)	0.89 (±0.39)	0.83 (±0.33)
% of time < 3 mmol/l (median, IQR)	0.00 (0.00-0.24)	0.00 (0.00-0.20)	0.00 (0.00-0.40)
% of time >10 mmol/l	1.26 (0.00-1.52)	0.00 (0.00-0.10)	0.00 (0.00-0.00)

Sheffield Children's Hospital (SCH) ACTH is measured as part of screening for AI, paired with an early morning cortisol, and at baseline (0 minutes) as part of the Short Synacthen Test (SST). We performed a cost-benefit study examining potential savings from a change in practice in which ACTH is measured only in patients who fail their SST.
Methods
We conducted a retrospective analysis of all SSTs performed at SCH between 2011-2019. Our diagnostic cut-off for a pass following adrenal gland stimulation with Synacthen is a peak serum cortisol of >429nmol/l. We determined the proportion of passed and failed SSTs. We used Pearson's correlation to determine the association between peak cortisol and ACTH. We calculated the potential cost savings of a change in practice where ACTH would be requested only in the event of a failed SST to help determine the cause of AI.
Results
We analysed 1275 SSTs, 905/1275 (71%) of which reached the diagnostic threshold for a pass. We found no correlation between baseline ACTH and peak serum cortisol ($r = -0.007$, $P = 0.836$). The analysis of an ACTH sample is currently £19.14. If our practice were to change to an ACTH measurement only in the event of a failed SST a cost saving of £17,322 would have been generated over the time period 2011-2019. We calculated, based on an increase in the number of SST requests over the study time period, a current cost saving of £2,456 per annum.
Conclusions
ACTH does not correlate with peak cortisol following Synacthen stimulation. Routine ACTH measurement in the diagnostic pathway for paediatric AI is not indicated, however it is important in the differentiation of primary AI from other causes. We recommend ACTH quantification is performed only after AI is confirmed by SST and believe this change in practice would lead to cost savings.

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P4

Current management of acute adrenal insufficiency related adverse events in children- results of an international survey of specialist centres

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Background
There is wide variation in the reported rate of acute adrenal insufficiency (AI) related adverse events (sick day episodes and adrenal crises) between centres.
Objective
Evaluate the level of consensus on the criteria that should be considered 'essential' for defining and managing adverse events associated with acute AI in children.
Methods
Active users of the International Congenital Adrenal Hyperplasia & International Disorders of Sex Development (I-CAH/I-DSD) Registries ($n = 66$), non-active users of I-CAH/I-DSD ($n = 35$) and the EuRRECa e-Reporting Registry ($n = 10$) were approached to complete an online survey.
Results
56 clinicians from 27 countries responded to the survey; response rates for the three Registry groups were 42 (65%), 11 (31%) and 3 (30%), respectively. Written corticosteroid management plans and one to one patient/parent education were provided by 54 (96%) and 51 (91%) clinicians, respectively; 33 (59%) provided steroid-aware emergency cards. 56 (100%) and 55 (98%) clinicians advised increases in glucocorticoid dosing (sick day dosing) in the event of fever or severe infection (eg. pneumonia). Less common indications for sick day dosing included vaccination and mild afebrile intercurrent illness, recommended by 17 (30%) and 9 (16%) clinicians, respectively. The most frequently reported sick day dosing regimen was tripling the total daily dose of hydrocortisone and administering 3 times daily, reported by 24 (43%) clinicians. 40 (71%) specified the duration of sick day dosing as ≥ 48 h for severe infections. Vomiting and diarrhoea were the most common indications for IM hydrocortisone, reported by 34 (61%) and 25 (45%) clinicians, respectively. Over 50% of respondents indicated that essential clinical criteria for adrenal crisis should include fatigue and nausea or vomiting and over 60% indicated that the criteria should include hypotension, hyponatraemia, hyperkalaemia and clinical improvement following parenteral glucocorticoids. A bolus parenteral injection of hydrocortisone and glucose infusions were the most frequently administered medications, reported by 50 (89%) and 32 (57%) of clinicians, respectively.
Conclusions
Although there is considerable variation in the definition and management of AI related adverse events in children amongst specialist centres, there is also good evidence of consensus that can be used to develop standardised criteria for developing benchmarks and facilitating care improvement.

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P5

A case of rare paediatric adrenocortical tumour presenting with virilisation

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Introduction
Childhood Adrenocortical tumours (ACTs) are rare neoplasms of the adrenal glands, accounting for 0.2% of all childhood cancers. Cases are mainly sporadic, but some mutations have been identified. ACTs are usually benign unilateral adenomas, but rare malignant carcinomas have poor prognosis. We present a case of adrenal insufficiency following a unilateral adrenalectomy for a functioning adrenocortical adenoma in a child.
Case
A 15 month old girl presented to a District General Hospital with a 3 month history of virilisation; coarse pubic hair, labia majora hypertrophy and clitoral enlargement. She had an uncomplicated birth and no prior medical conditions. There is significant family history of malignancy, including ACT in a maternal aunt. Initial tests showed raised serum androstenedione (21.6nmol/l) and testosterone (14.6nmol/l) along with high urinary adrenal androgen metabolites. A left sided adrenal hypoechoic solid mass was noted on ultrasound and staging CT confirmed a 3 cm lesion. She underwent an urgent left adrenalectomy and histopathology diagnosed a functional adrenocortical adenoma. A week later, she presented to our tertiary hospital with an unarousable episode and hypoglycaemia needing intramuscular glucagon. The hypoglycaemia screen showed low Cortisol (136nmol/l) and high ACTH (98.2ng/l). She was commenced on hydrocortisone maintenance for adrenal insufficiency. Subsequently, she had multiple admissions with hypoglycaemia requiring increasing doses of hydrocortisone and later on fludrocortisone was also required. Eventually, a cortisol day curve revealed that she is a 'fast metaboliser'. Further genetic testing detected TP53 mutation (Li-Fraumeni syndrome). Currently, she is thriving well on five times a day hydrocortisone and once daily fludrocortisone, with no further hypoglycaemic episodes. She is under regular paediatric endocrinology and oncology follow-up.
Discussion and learning points
Most childhood ACTs are functional and presentation largely depends on the extent and type of hormone secreted, with virilisation and hypercortisolism being common in girls. Adrenal suppression can occur after adrenalectomy requiring steroid replacement and close monitoring. There can also be a genetic component which increases the lifetime risk of cancers, requiring lifelong surveillance and family testing is recommended.

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P6

Diagnostic utility of cortisol responses to assess adrenal insufficiency using the GST – pilot study and literature review

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Background
The glucagon stimulation test (GST) involves administering an injection of glucagon and monitoring respondent levels of cortisol, growth hormone and glucose in the blood. The levels recorded are compared to current standard recommendations in order to offer a suggestion into growth hormone or cortisol deficiency. Many children who underwent the GST to investigate growth hormone deficiency (GHD) or prior to transfer to adult endocrine clinic failed to reach the adequate cortisol threshold outlined in the test, despite passing other tests to disprove cortisol deficiency. We conducted a pilot study and a literature review to investigate this.
Method
Our pilot study involved 14 children aged 3-18 years who underwent the GST between January 2016 and November 2020. All of the patients had previously shown adequate cortisol readings in alternative testing (Short Synacthen Test or ACTH stimulation test). Of these 14 patients, 5 achieved adequate cortisol

readings to pass the test ($\geq$430 nmol/l) and 9 did not reach the threshold so failed the test. Data was collected and comparisons were made between those who passed the test and those who failed. Specifically, we investigated the impact of blood glucose fluctuation and age on cortisol response. Additionally, a literature review was conducted using Embase and Medline looking at existing evidence.
Results
In our pilot study 9/14 patients failed the test, resulting in a 64% false positive cortisol deficiency rate. Mean peak blood glucose was higher in those who passed the GST compared to those who failed however this difference was not significant ($P=0.5448$). Extent of glycaemic fluctuation was significantly higher in those who passed the test compared to those who failed ($P=0.0022$). A strong negative correlation was seen between increasing age and peak cortisol ($r=0.74$).
Conclusion
Results from our pilot study and literature review suggest the need for the cortisol cut-off in the GST to be lowered and individualised to each patient, taking age into consideration. This study is limited by small sample size, so further research and ROC analysis is required in order to suggest more appropriate threshold values.

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P7

Growth characteristics of children presenting with congenital adrenal hyperplasia: An experienced of public sector hospital in Pakistan

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Introduction
Growth is considered as an important concern in patients with congenital adrenal hyperplasia (CAH). It is a group of recessive autosomal disorder which may develop due to genes mutation. In childhood, congenital adrenal hyperplasia (CAH) is considered as the most common inherited adrenal disorder. CAH can negatively affect the synthesis pathway of cortisol which leads to decrease cortisol level and a rise in the production of adrenocorticotrophic hormone. A high level of adrenocorticotropic hormone and a low level of cortisol in the body may result in early closure of epiphyseal and affects growth of the body. In this study we aimed to assess the growth characteristics in children diagnosed with congenital adrenal hyperplasia presenting at public sector hospital.
Methods
This descriptive study was conducted at public sector hospital, Karachi from November 2018 to May 2019. All patient of age between 5 to 15 years presenting with congenital adrenal hyperplasia were included by using non-probability consecutive sampling. However children with neural tube defects, Downs's syndrome and Horner's syndrome were excluded from the study.
Result
In this study 69 children with CAH were included. Out of which 41 (59.4%) were male. Mean age of children in our study was 7.40 ± 2.40. Approximately, 53 (76.8%) children suffered from short stature. Furthermore, children who were underweight constituted 19 (27.5%), overweight 10 (14.5%) and obese 34 (49.3%) of the population.
Conclusion
Our study reveals that congenital adrenal hyperplasia (CAH) significantly affects the growth characteristics in children. Regular follow-up, close monitoring and targeted therapy is required for all children diagnosed with congenital adrenal hyperplasia.

Keywords
Congenital adrenal hyperplasia, growth, Children, Short stature, Body mass Index.

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Bone

P8

A rare skeletal dysplasia-Progressive Pseudorheumatoid dysplasia—close mimicker of juvenile idiopathic arthritis

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A rare skeletal dysplasia-Progressive Pseudorheumatoid dysplasia—close mimicker of juvenile idiopathic arthritis

Introduction
Progressive pseudorheumatoid dysplasia (PPD) or spondyloepiphyseal dysplasia tarda with progressive arthropathy (SEDT-PA) is a rare autosomal recessive arthropathy of childhood involving the entire skeleton. Here we report first genetically proven case of PPRD from the country. Often mistaken as juvenile rheumatoid arthritis, however, the joint problems in juvenile rheumatoid arthritis are associated with inflammation, while those in PPRD are not. The definitive diagnosis is established in a proband with characteristic radiologic findings and biallelic pathogenic variants in *CCN6* (formerly *WISP3*) on genetic testing.
Case report
7½ years old, vaccinated boy, having weight of 12.5 kg(SDS-3.0) and height of 104 cm(SDS -4.5) with normal vitals and no significant birth and developmental history, referred to our endocrine OPD for workup of short stature in 2019. He had restricted movements in small joints of hands bilaterally and painful right knee joint for last two years. Child had been extensively worked up for juvenile idiopathic arthritis and been given multiple oral NSAIDs. No familial disorder of joints or skeleton in the family. On examination a young cooperative boy of extreme short stature and lean built. His gait was normal with restricted movements in all PIP and DIP joints of bilateral hands and spindle shaped deformities of all fingers. Spine and TMJ were normal. His Hb was 11.9, TLC 9.1 and platelets were 361 with negative inflammatory markers including ESR and CRP. Serum biochemistry, renal functions and thyroid profile were within normal range. Screening for celiac disease TTg IgA and IgG were negative and he was found to be moderately growth hormone deficient on Insulin tolerance test (ITT) .Skeletal survey showed large epiphysis and widened metaphysis of the metacarpals/metatarsal and phalanges of hands showing periarticular osteopenia without erosion. Spine radiographs showed inferior beaking, and platyspondyly typical for PPRD.fig Two pathogenic variants identified in WISP3 gene, confirming the diagnosis of PPRD.
Conclusion
Creating awareness regarding this rare form of skeletal dysplasia is crucial to avoid extensive workup and use of multiple drugs for JIA as well as to offer early management including orthopedic interventions.

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P9

Vitamin D inadequacy in childhood cancer survivors: prevalence and risk factors

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Background
Childhood cancer survivors (CCS) are at high risk of 25-hydroxivitamin D (25(OH)D) inadequacy and the lack of a consensual definition has hampered its epidemiological study. Despite international recommendations, bone health and vitamin D inadequacy (VDI) are still quite undervalued, even in a high-risk population as CCS, due to disease treatment, physical limitations and insufficient solar exposure.
Objectives
Our aims were to determine the prevalence of plasma 25(OH)D inadequacy in CCS in a tertiary pediatric center and to identify potential risk and protective factors for VDI.
Material and Methods
A retrospective cross-sectional cohort study was performed in Portuguese survivors under the age of eighteen diagnosed, followed and treated for cancer from January 1, 2016 to April 30, 2021. 25(OH)D status was defined according to Munns *et al* Global Consensus: deficiency (<12 ng/mL) and insufficiency (12-20 ng/mL). Bivariate analysis was carried out to study the impact of age at diagnosis, pubertal stage, cancer type and treatment exposures.
Results
Of the 219 CCS recruited, 94 (43%) had at least one routine 25(OH)D blood screening, with median age 7.71 years, interquartile range: 10; 55% males. Of these, 25(OH)D inadequacy was highly prevalent (58.5%) among cancer survivors: 8 (14.5%) deficiency and 47 (85,5%) insufficiency; only 39 (70.9%) of them underwent supplementation. Median of 25(OH)D levels was 17.0 ng/mL (IQR: 7.0; minimum: 4.0). The most frequent oncologic diagnoses included lymphoproliferative disorders (39%), brain tumors (41%; 13% gliomas), solid non-brain tumors (15%) and Langerhans cell histiocytosis (4%). Thirty percent of survivors had at least one sequel, being hemiparesis (5%) the most prevalent one; 13% had metastatic disease. There was a positive and statistically significant correlation between plasma 25(OH)D level and age at diagnosis ($P < 0{,}001$; δ: 0.484). Concerning pubertal stage, cancer type and treatment exposures, no statistically significant associations were found.

Conclusion
The prevalence of 25(OH)D inadequacy was even higher than expected in this population, considering international literature and country latitude. This reinforces the necessity to value bone health by diagnosing VDI, ensuring therapeutic supplementation and monitoring in risky populations.

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P10

Rule of parathyroid hormone and vitamin D investigations in metabolic bone disease of prematurity diagnosis and management

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Background
Metabolic bone disease of prematurity (MBDP) is characterized by decreased bone density as a result of insufficient mineral deposition in the bones of premature babies. Although the primary cause of MBDP is different from one case to another; either hypocalcaemia or hypophosphataemia, the main current practice is to treat it with phosphate supplements.
Objectives
To emphasize the rule of parathyroid hormone and vitamin D investigations in MBDP diagnosis and management.
Methods
Data were collected retrospectively between March 2019 and June 2020 from the patientś notes and hospital electronic systems in a UK tertiary neonatal unit. Babies born at 29 weeks or less with a diagnosis of MBDP at discharge were included in the study.
Results
In total, twelve babies were included with different gestational ages as illustrated in table 1. Five of them did not show any improvement over the routine treatment with phosphate supplements at 1 mmol/kg once daily. Therefore, PTH and vitamin D levels were investigated; the earliest of which was done after 4 weeks from starting the treatment. Three out of five babies had high PTH and low vitamin D. Therefore, phosphate supplements were stopped and calcium was started. Subsequently, the parathyroid hormone levels normalized shortly after starting calcium supplements. Furthermore, the MBDP incidence was noted to be related to high diuretic use, corticosteroids, low gestational age and prolonged use of parenteral nutrition.
Conclusion
MBDP incidence in our local unit was 21% during the study period. Quarter of the patients had hyper-parathyroidism as a result of either inappropriate initial treatment with phosphate supplements or preliminary low calcium or vitamin D. Although the main aim is to prevent the MBDP incidence, consideration of earlier investigation of both parathyroid hormone and vitamin D is of an equal importance for guidance of the appropriate treatment course of MBDP.
Abbreviations
MBDP: metabolic bone disease of prematurity.
PTH: parathyroid hormone.

Table 1 Shows the classification of included babies according to their gestation age at birth.

Gestational age	23 weeks	24 weeks	25 weeks	26 weeks	28 weeks	29 weeks
Number	1	2	5	1	2	1

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Diabetes

P11

Type 1 Diabetes: the Laos perspective

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Introduction
In many lower-middle income countries (LMICs), poverty, insufficient infrastructure and lack of universal health coverage affect type 1 diabetes (T1D) outcomes. Limited insulin and unavailability of blood glucose monitoring supplies contribute to poor glycaemic control and T1D complications that adversely affect mortality and morbidity. Laos is a LMIC in Southeast Asia (SEA) with a population of 7.3 million. Its GDP per capita is USD 2,534 of which only 2.5% represent government healthcare spend and does not provide for diabetes treatment. No known Laotian had previously survived T1D. Since 2016, a programme started by a non-government organisation (NGO), Action4diabetes (A4D), has been providing insulin, blood glucose monitoring kits, HbA1c tests and emergency hospital funds for Laotian children and young people (CYP) with T1D, including education and training for healthcare professionals, in partnership with the Laos government. We report the first data on demographics and clinical outcomes of Laotians with T1D enrolled to-date.
Methods
Data from 2016 to 2021 were reviewed including gender, age and presentation at diagnosis, HbA1c and hospital admissions.
Results
There were 53 CYP (31 male; 58%) diagnosed with T1D at a mean (SD) age of 10.4 (4.2) y, of whom 31 CYP (58%) presented in DKA at diagnosis. Forty-four of the 53 CYP (83%), currently aged 12.9 (4.8)y, remain on active follow-up (24 male; 55%), and have had T1D for 2.4 (2.3)y. From 2016 to 2021, mean HbA1c was 9.0% (75 mmol/mol) overall, and 8.5% (69 mmol/mol), 8.1% (65), 9.1% (76), 9.8% (84), and 7.7% (61) among the CYP aged 0-5y, 6-10y, 11-15y, 16-20y, and 21-25y, respectively. There were a total of 39 hospital re-admissions for DKA (0.3/person/y), 9 re-admissions for severe hypoglycaemia (0.07), and 9 re-admissions for other reasons (0.07).
Conclusions
This is the first report on T1D care in Laos spanning 2016 to 2021. There is a need for more global efforts to improve T1D care outcomes in Laos and other LMICs in SEA. Close partnership between NGOs and governments has enormous potential in developing sustainable and locally owned solutions for improving diabetes care in CYP with T1D in these LMIC.

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P12

Government partnership working in Southeast Asia low-middle-income countries and Action4Diabetes improves Type 1 diabetes care

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Introduction
Globally, the main cause of mortality of type 1 diabetes (T1D) is lack insulin access. There is minimal data of health outcomes for T1D in low-middle-income countries (LMICs) in South-East Asia (SEA) where government funding of insulin and blood glucose monitoring kits either do not exist or is limited. Action4Diabetes (A4D) is a non-government organisation (NGO) initiated in 2016 and supports children and young people (CYP) with T1D in five countries - Laos, Malaysia, Vietnam, Cambodia and Myanmar in the SEA region. A4D is the only UK-registered NGO that provides comprehensive partnership programmes with local hospitals through a Memorandum of Understanding (MOU) with the governments in Laos, Vietnam and Cambodia which guarantees ongoing supplies of free insulin, blood glucose meter kits, HbA1c tests and hospital emergency funds.
Objectives
The objective is to determine the Hba1c outcomes in the five SEA countries between 2020-2021 through A4D partnership working with local government hospitals.
Methods
We reviewed with local healthcare professionals the latest HbA1c of 383 CYP with T1D between 2020 to 2021 who remained active in the A4D programme. The duration of support by A4D for these patients ranged from 3 to 60 months. Patients were excluded if they were lost to follow up or had died.

Conclusions
The average HbA1c of CYP with T1D under the A4D programme within the five SEA countries was high at 83 mmol/mol (9.7%). In many low-to-middle income countries, lack of infrastructure and universal health coverage adversely affect T1D outcomes. A4D partnering with local government to support CYP with T1D from diagnosis to adulthood is the first step to improving T1D outcomes in SEA.

Results:

Country	No. of Type 1 patients (n= 383)	*Mean Age in years (range)	HbA1c mmol/-mol (%) between 2020-2021
Myanmar	80	11.1 (1,17)	67 (8.3)
Laos	45	13.3 (3, 24)	69 (8.4)
Vietnam	48	9.7 (3,17)	79 (9.4)
Cambodia	181	17.9 (8, 29)	95 (10.8)
Malaysia	29	14.7 (4,26)	82 (9.6)
Summary	**383**	**14.7 (1,29)**	**83 (9.7)**

**this represents the mean age (range-minimum, maximum)) of current active patients recruited to the A4D programme in 2020-2021*

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P13

Increased diabetic ketoacidosis at presentation of type 1 diabetes mellitus – A result of the COVID-19 pandemic or longer-term increasing trend?

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Background
Reports from several countries have suggested an increased incidence of diabetic ketoacidosis (DKA) at presentation of type 1 diabetes mellitus (T1DM) during the COVID-19 pandemic. Published data on this from the United Kingdom is sparse. We examined the frequency and severity of DKA at diagnosis of T1DM in children presenting to a university hospital during the first year of the pandemic in comparison to preceding years.
Methods
In England, the first COVID-19 national lockdown began on 23/03/2020. The first year of the pandemic was defined as 23/03/2020 to 22/03/2021. Data was compared to the four preceding years, each starting on 23rd March. All children (<18 years) presenting to University Hospital Southampton NHS Foundation Trust with a new diagnosis of T1DM were included. Children transferred into the regional Paediatric Intensive Care Unit from other hospitals for escalation of care were excluded. Data was extracted from electronic case records, including presence and severity of DKA (defined using the British Society for Paediatric Endocrinology and Diabetes 2020 guideline), HbA1c, weight and height. Weight and body mass index (BMI) standard deviation scores (SDS) for age and sex were calculated using British 1990 reference data.
Results
During the first year of the pandemic, 30 children presented with T1DM, which was similar to the preceding 4 years (n=19-28 per year). 53.3% presented with DKA during the pandemic; however this proportion had increased each year since 2017/8: 32.1% in 2016/17, 17.9% in 2017/8, 39.1% in 2018/19, 42.1% in 2019/20 (p trend 0.022). There was a similar increasing trend for severe DKA (pH <7.1 or bicarbonate <5 mmol/l): 10.7%, 10.7%, 13.0%, 15.8%, 33.3% for each consecutive year from 2016/17 to 2020/21 (p trend 0.020). Age, sex, HbA1c, weight SDS and BMI SDS did not differ by year of presentation.
Conclusion
DKA was present in over half of children presenting with T1DM during the COVID-19 pandemic. There appears to be an upward trend in the frequency and severity of DKA at T1DM diagnosis, which predated, but continued to increase, during the COVID-19 pandemic. A novel education strategy to facilitate T1DM diagnosis before DKA might be beneficial in reversing this trend.

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P14

Level 3 Carbohydrate counting at diagnosis of Type I Diabetes Mellitus in children: How does it affect HbA1c?

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Introduction
National guidance recommends Level 3 carbohydrate counting (L3CC) is delivered within 2 weeks of diagnosis of Type I Diabetes Mellitus (T1DM) (NICE, 2015). This was introduced at Derbyshire Children's Hospital in 2017. This service evaluation aimed to assess the impact of this on patients' blood glucose, by recording HbA1c levels at quarterly intervals over 6 months.
Methods
A comparison of quarterly HbA1c in children that received L3CC at diagnosis were compared to a historical control group of those that did not, being diagnosed prior to the implementation of L3CC. HbA1c results were taken during attendance at multidisciplinary clinics. Where exact quarterly dates were not available, the closest time period either side was taken.
Results
HbA1c readings for 89 children (45 females, 44 males; mean age 9.5years) were included, 48 children received the intervention and 41 did not. The mean HbA1c at diagnosis were similar (105 mmol/mol and 97 mmol/mol for the control and intervention groups respectively; P=0.06). HbA1c reduced by 46% in both groups after 3 months and was significantly lower in the intervention group (56 mmol/mol vs 52 mmol/mol respectively; P=0.008). HbA1c remained significantly lower in the intervention group at 6 months (56 mmol/mol vs 48 mmol/mol; P=0.001).
Conclusion
Introduction of L3CC within 2 weeks of diagnosis of T1DM in children has beneficial effects on glycaemic control at 3 and 6 months post diagnosis compared with traditional care. HbA1c was significantly lower following L3CC, and children reached the target HbA1c of 48 mmol/mol, which minimises their risk of long term complications (NICE, 2015).

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P15

Patient experience of home and drive through HbA1c measurement during the COVID 19 pandemic

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Background
Prior to COVID-19, HbA1C was performed in clinic as a point of care test. As a service development project driven by the changes to our service from COVID-19 we offered either a hospital drive through point of care HbA1C test or the validated VAMS collection method to obtain HbA1C at home.
Objective
Research ethics approval was obtained to assess patient/carer acceptability of these collection methods.
Methods
Drive through HbA1C appointments were offered to all patients under our care. Fifty home HbA1c VAMS tests kits were sent to those were unable to attend the hospital. A survey asking children and young people (CYP) and their parents to score their agreement with statements on a 7-point Likert-type scale was distributed to the 280 families in our diabetes service.
Results
We received 65 complete responses. 8 respondents had not had either home or drive through HbA1C tests. Ten respondents used home HbA1c tests. Overall 90% found the home test kits easy to use (sampling, ease of use, instructions convenience and satisfaction) overall. Fifty percent of CYP found the home HbA1C test less painful than hospital HbA1C measurement. Forty seven respondents attended for drive through HbA1c. Fifty percent were not concerned about attending the hospital during the pandemic, 89 % found the procedure convenient, 34% preferred point of care testing over home HbA1c. The majority of the written feedback reported the service to be convenient and efficient, with an overall 97% satisfaction with the service. However patients who lived some distance from the hospital site felt a home HbA1C testing option would be preferable to driving to the hospital for a 5 min appointment.

Conclusion
Both modes of measurements had 90% or above ratings for satisfaction and convenience. In future we plan to continue some remote clinics; this data can be used to further develop the HbA1C testing options we offer.

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P16

Children and young people with type one diabetes and their families experience of remote clinics

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Background
Children and young people (CYP) with Type 1 diabetes are offered 4 face to face appointments annually. During the COVID-19 pandemic these were delivered virtually.
Objective
We conducted a survey to assess patient and carer satisfaction with the remote diabetes service.
Methods
Research ethics approval was obtained. The survey was distributed to 280 CYP and their families; one response per family was collected. Data on; age, time since diagnosis, method of diabetes management, feedback on video "attend anywhere" consultations and suggestions for improvements were recorded.
Results
We received 65 responses; 12 from CYP and 53 from parents/carers. Mean age of CYP was 11.4 years; mean time since diagnosis was 5.4 years. Sixty eight percent of respondent's used an insulin pump and 83% CGMS or Libre sensor. Ninety three percent were able to connect to the attend anywhere platform easily and maintain good internet connection (89.0%). Eighty seven percent reported good interaction with healthcare professionals and 89.0% felt able to raise concerns remotely. Fifty eight percent of respondent's wanted to continue video consultations following the pandemic with 33% wanting to return to 100% face to face appointments. Thirty six percent wanted at least 2 face to face consultations moving forward whilst 11.4% did not want to be seen face to face after the pandemic. >Written feedback on remote consultations was variable between families. Whilst some carers found remote consultations more convenient and reported that clinician's time keeping was better in the virtual setting many families reported that it was difficult to build good rapport and engage during the virtual consultations and that appointments often felt impersonal. A key theme was CYP needing some face to face appointments in order to build a trusting relationship with healthcare professionals.
Conclusion
Whilst from the outset it may seem that it is more convenient for carers and the MDT to deliver a mix of face to face and virtual appointments, feedback demonstrated that people's experiences with our remote service was highly variable. It is therefore important to deliver individualised care plans that meets every patient's specific needs.

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P17

Do hospital admissions improve outcomes for children and young people with poor diabetes control?

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Introduction
Achieving an HbA_{1c} of less than 48 mmol/mol minimises the risk of complications in children and young people with type one diabetes. Elective admissions to hospital are one option employed to improve glycaemic control in patients with an HbA_{1c} above target. There is however limited evidence to support such admissions. We aimed to retrospectively compare glycaemic control between patients electively admitted to hospital to stabilise their diabetes with a matched control group.
Methodology
Records of all children and young people with type one diabetes, admitted for the purpose of stabilisation of poor glycaemic control over a one-year period at our centre were reviewed. Admitted patients were matched with a control patient receiving support in the community, based on sex, age and HbA_{1c}. Measures of HbA_{1c}, average blood glucose and number of blood glucose tests at admission, were compared to values at three, six and twelve months after admission using t-tests.
Results
Twelve children (mean age 13.1years) were electively admitted for diabetes stabilisation during the study period. The control group did not differ in baseline demographics to those admitted. Mean HbA_{1c} of the admitted group decreased from 84.8 mmol/mol to 76.8 mmol/mol twelve months after admission, this was a similar improvement to the control group (HbA_{1c} decreased from 80.4 mmol/mol to 69.0 mmol/mol, $P=0.80$). Admitted patients and controls demonstrated similar changes in mean blood glucose (admitted -1.82 mmol/l vs controls -1.28 mmol/l, $P=0.74$) and number of blood glucose checks (admitted -0.44 vs controls -0.73, $P=0.92$) twelve months after admission. When stratified by HbA_{1c}, those with $HbA_{1c} \geq 80$ mmol/mol demonstrated a trend towards a greater improvement in HbA1c at twelve months than those with $HbA_{1c} < 80$ mmol/mol (-18.8 mmol/mol vs +2.7 mmol/mol, $P=0.29$). Stratification by sex, showed females had a greater improvement in HbA_{1c} twelve months after admission than males (-23.4 mmol/mol vs +13.4 mmol/mol, $P=0.05$).
Conclusion
Elective admissions appear to lead to a modest improvement in HbA_{1c} one year after admission, however this is similar to the improvements seen in non-admitted patients with comparably poor glycaemic control. Admissions may be more beneficial to specific strata of the population, highlighting the need for careful selection of patients for diabetes stabilisation admissions.

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P18

High-risk proliferative retinopathy and macular oedema in an adolescent boy with thiamine-responsive megaloblastic anaemia

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Thiamine-Responsive Megaloblastic Anaemia (TRMA) is a rare autosomal recessive disorder emerging due to mutation in the thiamine transporter 1 gene. It presents with sensorineural hearing loss, non-immune diabetes mellitus and megaloblastic anaemia. Ocular manifestations of TRMA described so far include optic atrophy and cone-rod retinal dystrophy. This case-report presents an adolescent British-Pakistani boy with TRMA, who was unexpectedly diagnosed with bilateral severe proliferative retinopathy and macular oedema, just 3 months after being diagnosed with diabetes. His parents are first cousins. He was diagnosed with bilateral sensorineural hearing loss at 2 years of age. He subsequently presented at 14 years of age with mastoiditis, when he was also found to be in diabetic ketoacidosis (DKA). Tests for islet-specific autoantibodies were negative. First retinal screening (3 months after presentation with DKA) identified bilateral high-risk proliferative retinopathy and macular oedema. At the same time, he was admitted with breathing difficulty and was found to have anaemia, thrombocytopaenia and reticulocytopaenia. Peripheral smear demonstrated marked poikilocytosis. Further evaluation for pancytopenia revealed normal clotting, lactate dehydrogenase, vitamin B12, folic acid and ADAMTS-13 levels and test results for autoantibodies and PCR for several viruses were negative. Bone marrow examination revealed erythroid dysplasia and numerous ring sideroblasts, and this eventually led to the diagnosis of TRMA. Red-cell thiamine level was 60 nmol/l (67–200). He was started on high-dose thiamine therapy (50 mg/day). Haemoglobin, red cell and platelet count improved and normalised within 3 weeks. Red-cell MCV increased from 79.9 to 100 fL. The patient is homozygous for a pathogenic SLC19A2 nonsense variant NM_006996.2:c.196G>T p. (Glu66Ter) and both parents are heterozygous for the same mutation. He has had pan-retinal photocoagulation and his diabetes is better controlled since starting thiamine, though he continues to require insulin therapy. Proliferative retinopathy within 3 months of diabetes diagnosis in adolescence, is highly unusual. It may be due to the combined effect of intracellular thiamine deficiency and severe hyperglycaemia.

Table 1 Libre data and insulin doses pre-Kaftrio, immediately post Kaftrio and 5-13 months after starting Kaftrio.

Investigation	Patient's results
Haemoglobin	40 g/l
RBC count	1.49 * 10^12/l
Mean corpuscular volume	79.9 fL
Platelets	42 * 10^ 9/l
WCC	4.1 * 10^9/l
Reticulocyte count	4 * 10^9/l

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P19

Frimley Park Hospital Quality Improvement Initiative 2019-2020: Safe management and discharge of newly diagnosed children and young people with diabetes

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Introduction
Frimley Park Hospital, Surrey had been a negative HbA1c outlier for 3 consecutive years. The Children's and Young People's (CYP) diabetes team embarked upon the RCPCH National CYP Diabetes Quality Improvement (QI) Programme in November 2019. There was little qualitative data on ward nurse education, however, experience revealed engagement in staff training was the main barrier. Although regular education sessions were available to ward staff, attendance was generally poor, and gaps were observed notably in staff knowledge and skills.
Aims
The team decided to optimise the safe discharge of newly diagnosed CYP with diabetes from the paediatric ward. We believe important key messages relayed from nursing staff during patients' admissions form a key role in patients' education, confidence, and experience.
Methodology
Fishbone analysis highlighted many essential factors to consider, such as staff knowledge, practical skills, set up of devices, resources, and patient pathways. We therefore prioritised ward staff education in terms of educational interventions. Data collection was through written or online quizzes. Confidence questionnaires both pre- and post implementation of the updated education, helped formulate scores.
Results
A total of 57 nurses were invited, 23 participated and revealed they were most confident with insulin injection administration, but least with blood glucose meter use. Nurses scored 20/25 pre-intervention and 23/25 post-educational intervention. A total of 30 doctors were invited and 27 participated at different intervals. Doctors revealed they were most confident in managing hypoglycaemia and least confident in carbohydrate counting on the ward. Doctors' pre-intervention scores were 3.8/5 and 4.5/5 post-intervention. The data showed an improvement in both nursing staff and doctor's knowledge and confidence in managing newly diagnosed CYP with Type 1 diabetes post-educational sessions. Other interventions included: updating ward guidelines, improved patient pathways, electronic discharges and prescriptions, introduction of Level 3 Carbohydrate Counting with dose adjustment prior to discharge, and provision of age banded insulin to carbohydrate ratio reference sheets to assist doctors with insulin dose calculation on diagnosis.
Conclusion
During the QI process we have learned that the task can be greater than anticipated, although with motivation, communication and teamwork, our goal was achieved.

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P20

Does diabetic ketoacidosis at diagnosis of type 1 diabetes mellitus affect anti tissue transglutaminase immunoglobulin A (tTG-IgA) levels?

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Background
Current guidance recommends screening for coeliac disease (CD) at diagnosis of type 1 diabetes mellitus (T1DM) using measurement of serum anti tissue transglutaminase immunoglobulin A (tTG-IgA). It is recognized that tTG-IgA levels can fluctuate and there are reports of transient rises in tTG-IgA levels in response to acute stress, such as infection and acute coronary syndrome. The effect of diabetic ketoacidosis (DKA) on tTG-IgA has not been reported. We investigated whether serum tTG-IgA levels were higher in children at T1DM diagnosis, who presented with DKA compared to those not in DKA.
Methods
Electronic patient records for children (<18 years) presenting with a new diagnosis of T1DM to University Hospital Southampton NHS Foundation Trust between 01/01/2017 and 30/05/2020 were reviewed. DKA was defined using the British Society for Paediatric Endocrinology and Diabetes 2020 guideline (blood pH<7.29 or bicarbonate <15 mmol/l). tTG-IgA was considered raised if it was above the upper limit of normal (ULN) for the assay.
Results
77 children presented with T1DM during the study period (48.1% male, mean age 9.73 years (SD 4.21)). 32.5% presented with DKA. One child had pre-existing CD. tTG -IgA was assessed at acute presentation in 69 (90.8%) children. Raised tTG-IgA was found in 6 of 69 (8.7%) children, but with similar frequency in children with (4.5%) and without DKA (10.6%, $P=0.66$). Total tTG-IgA did not differ between children presenting with and without DKA ($P=0.72$). 3 of the 6 children with raised tTG-IgA had CD diagnosed without biopsy (tTG-IgA 87-225 x ULN). 2 children with moderately raised tTG-IgA (3.8-4.7 x ULN) were diagnosed with CD following intestinal biopsy, and one child (not in DKA at diagnosis) had a tTG-IgA 3.0 x ULN, which had normalized 6 months after diagnosis of T1DM.
Conclusions
Diabetic ketoacidosis did not affect serum tTG-IgA levels in our patient group. Given the high frequency of undiagnosed CD at presentation of T1DM, screening should not be delayed until recovery from DKA, but the potential for normalization of a raised tTG-IgA should be considered in the further investigations/referral of child with a moderately raised tTG-IgA.

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P21

A single-centre evaluation of telemedicine consultation and associated CO2 emissions for children and young people with diabetes

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Background
Telemedicine use has increased rapidly during the COVID-19 pandemic, replacing many face-to-face (FTF) consultations. FTF consultations are associated with increased CO2 emissions (CO2em) from travel to clinics. This study evaluates the triple bottom line of children and young people's (CYP) and parent or guardian experience of a new telemedicine service, estimated CO2em saving from reduced travel and cost saving to families.
Methods
Data were collected via telephone interview from CYP and their families, looked after by a single paediatric diabetes service and who had recently had a telemedicine consultation. Parents and young people were contacted by telephone after their telemedicine consultation and data regarding their experience collected via semi-structured interviews. An estimate of CO2em was calculated based on published average vehicle CO2em and distance travelled. Families were also asked to estimate how much a FTF appointment would have cost them in travel expenses including petrol and parking charges.
Results
42 telephone interviews with CYP, age 6-18 years, and their families were conducted. 64% of interviewees described the video call quality as being just as good as FTF, with 36% describing it as satisfactory but not as good as FTF. Overall, 45% interviewed described preferring remote consultation, 26% expressing no preference and 29% preferring FTF consultation. 93% of interviewees reported that they would be happy to use remote consulting again. Average CO2em was calculated at 1.65 kg per clinic visit per patient for travel to F2F appointments. With an expected 4 clinic visits per patient per year this equates to 6.62 kg CO2 emitted via travel per patient year. Median reported cost saving from not coming to a F2F clinic was 9.40GBP.
Conclusions
A large reduction in CO2em is achieved in reducing travel to appointments. Remote consultation allows for lower CO2em per clinic review with good levels of patient satisfaction reported. Some aspects of FTF diabetes consultation such as

HbA1c measurement are more challenging via telemedicine consultation, however wearable glucose monitoring devices may offer alternative measurements.

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P22

Comparison of measurement, mean and median of HBA1c during COVID-19 pandemic and previous year

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There is little evidence of glycaemic control changes in Paediatric patients with diabetes during pandemics or natural disasters. We were interested in analysing and comparing the HbA1c values in children and young people with diabetes at West Hertfordshire NHS trust before the covid-19 pandemic in 2019-2020 and during lockdown in 2020-2021. Our hypothesis was that there would be a deterioration in HbA1c outcomes and a reduction in the number of tests done in 2020-2021. We assessed number of HbA1c measurements, mean and median on 204 patients under 19 years of age and the impact of using innovative ways of measuring HbA1c. Results showed a significant decrease in number of Hba1C tests during the months of lockdown, from 655 pre lockdown to 450 (p0,005) after. There was also a decrease in the number of tests done per patient, with average of 3.31 tests before and 2.11 after. However, significant increases in HbA1c testing were seen during the period when innovative ways of drive-through and walk-in clinics were introduced tripling and doubling number of measurements, respectively. The mean HBA1c was significantly lower from March 2020 to March 2021 at 65.23 mmol/mol compared to 69.93 mmol/mol in the previous year (p0.019). In conclusion, the innovative ways of testing HbA1c measurement, can be of value during natural disasters and pandemics but may also be of benefit and add flexibility for the patients as the diabetes services are reconstructed post pandemic restrictions. We cannot say for certain what improved the HbA1C significantly during lockdown. One hypothesis is that the lower mean HbA1c values were because patients with better glycaemic control historically were more likely to attend for the HbA1c tests. We had seen a higher percentage of patients with a mean HbA1C of more than 80 mmol/mol (12% vs 29%) in the previous year and patients that did not attend in the year of lockdown had a considerably higher mean 76.8 mmol/mol (p:0.3). However, we would need further individual patient analysis to confirm this. We also propose that it would be helpful to conduct a survey of patients and their parents to find out other contributing factors.

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P23

A real-world approach of delivering virtual paediatric diabetes consultations during the COVID-19 pandemic

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The use of digital technology to improve accessibility and efficiency of services has been recognised and telemedicine has been increasing over recent years, particularly for patients with chronic conditions such as diabetes. The onset of the COVID-19 global pandemic rapidly accelerated the use of virtual consultations into everyday practice. The aim of this study was to assess feedback from paediatric diabetes patients and their parents regarding virtual consultations. The study was performed in a district general hospital during the first COVID-19 lockdown in the UK. An electronic survey was sent to patients following their virtual consultation. A total of 22 virtual clinics were held between 1st May 2020 to 1st October 2020. 37 feedback forms were obtained during this time period from parents (31) or children and young people (6). Of those surveyed, 86% recommended video consultations to be part of their diabetes care. Qualitative data showed reduced travel time, comfort, reduced need for parking and convenience as the highest areas improved through video consultations. Clinical care was shown to be positive and addressed patients concerns, 84% of those surveyed reported that the appointment was about what they wanted it to be about. This study shows how technology can be effectively used for multi-disciplinary team working and co-ordinating patient care. Challenges are faced however through health inequalities leading to difficulties accessing technology and digital exclusion. The recent NPDA 2021 shows that social deprivation is a significant factor affecting glycaemic control. A previous study has also shown that children from more deprived areas are less likely to download and have poorer HbA1c levels. It is important to consider the ongoing implications for patients having access to technology to be able to attend virtual clinics and efforts need to be made to try and reduce health inequalities. Virtual consultations have provided a solution to the challenges of patient access faced through the COVID-19 pandemic. Although there are benefits highlighted, it is important to conduct further research into the impact of this for both patients and professionals and to ensure systems are in place to create the best virtual health service experience.

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P24

Does low-glycaemic index diet affect glycaemic control, diet adherence and life quality of type 1 diabetic children and young people?

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Background
Nutrition of the children and young people with type 1 diabetes mellitus is considered a major aspect of glycaemic control and it represents a big challenge in their management. Among the different perspectives of nutritive interventions for diabetic children, there has been a debate over the recommendation of low glycaemic index diet for them. There has been debate over the efficacy of Low GI foods on diabetic patientś blood glucose control. Nevertheless, Evidence shows that these foods may positively contribute to the long-term glycaemic control, HbA1C levels, blood glucose variability and postprandial blood glucose levels. Table 1 explains the idea of glycaemic index of different foods.
Objective
To review the literature available to establish the relationship between low GI diet and different aspects of type 1 diabetic patientś management; including glycaemic control, diabetic complications, dietary variability and quality of life.
Methods
An electronic search of the database was conducted and included all the studies that assessed the effect of low glycaemic index diets on disease control and quality of life of children and young people with type 1 DM.
Results
The results showed that the low glycaemic index diets were associated with better glycaemic control in terms of significant improvement of HbA1c and postprandial glucose variability and excursions. Moreover, patients showed better adherence to the dietary instructions. Considering quality of life in diabetic patients, there was some evidence that the LGI diets were associated with better quality of life. However, most of the studies depended on retrospective dietary records which may have shown reporting bias.
Conclusion
Despite the long-standing debate over the effectiveness and applicability of the glycaemic index for management of type 1 diabetic children, evidence showed better glycaemic control, postprandial glucose excursion and improved blood glucose variability with low glycaemic index diets.

Table 1 illustrates both glycaemic index and glycaemic load of different meal components.

Food	Amount (gm)	CHO (gm)	Predicted GI	Contribution to the meal GI	Glycaemic load
Lentils	47	25	43	13.5	3.375
Rice	58	50	83	52.4	26.2
Carrots	100	5.7	104	7.5	0.4275
Apple juice	200	23.6	53	15.8	3.7288
				89.2	**33.7313**

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P25

A small change leading to a big impact

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Background
"Diabetes (type 1 and type 2) in children and young people: diagnosis and management" guideline (NICE NG18, 2015) stipulates following "Coeliac

disease: recognition, assessment and management" guideline (NICE NG20, 2015) for follow up children and young people (CYP) with diabetes and coeliac disease. NG20 advocates against checking coeliac antibodies on yearly basis if compliance with gluten free food is confirmed by dietary review. In 2016, we audited annual review of CYP with type 1 diabetes and coeliac disease compliance with NG20. The results showed that 80% of these CYP had coeliac serology checked (20% compliance with standard). Action plan included raising awareness about NG20 and changing diabetes annual review investigations panel in pathology requesting system.

Aim

Re-audit to assess progress following the implementation of changes based on the results and recommendations of the initial audit.

Standard

NICE NG20: CYP with coeliac disease should have annual review of symptoms, weight and height measurement and dietitian assessment of compliance with gluten free food. Routine serologic testing is not indicated.

Methodology

Patients with T1DM and coeliac disease attending the Paediatric Diabetes clinic in our hospital between 1/4/2018 to 31/3/2019 were identified, and their annual review processes data was extracted from electronic patient records.

Results

The re-audit showed 100% compliance with review of symptoms, weight & height measurement, and serology testing. Compliance with dietetic review was 77.78% attributed to limited dietetic resource availability.

Conclusion

A small change in pathology investigation request profile increased compliance with coeliac serology testing standard from 20% to 100%.

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P26

HbA1c and attendance before and after transition to adult diabetes service: a transition audit

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Background

The transition period is a challenging time for adolescents and is frequently associated with deterioration of HbA1c, decreased attendance, and disengagement from services. Two London hospitals both have existing transition programs to facilitate the movement of patients with diabetes from paediatric to adult care services.

Aim

This audit aimed to assess mean HbA1c values, HbA1c monitoring frequency, and appointments offered and attended in the year before and after transition.

Method

For diabetes patients transitioning to the adult services between February 2017 and March 2019, HbA1c measurements and number of appointments data in the year pre- and post-transition were recorded. Audit standards were developed from relevant paediatric and adult NICE guidelines.

Results

A total of 33 patients underwent transition and one patient had their care transferred to their GP. Three (9.1%) of those patients who transitioned did not attend any clinics in the year after transition and were lost to follow up. Following transition, no significant change in mean HbA1c was seen (74.1 ± 23.6 vs 76.2 ± 24.6 mmol/mol, $p > 0.05$), but there was a significant reduction in mean frequency of HbA1c monitoring (3.1 ± 1.4 vs 1.3 ± 0.8, $P < 0.001$). A significant reduction in appointments offered (8.3 ± 2.4 vs 5.8 ± 2.7, $P < 0.001$) and attended (5.1 ± 3.1 vs 3.7 ± 2.4, $P < 0.001$) was seen after transition. Despite this there was no significant difference in attendance rate for the cohort as a whole ($67.5 \pm 28.5\%$ vs $66.4 \pm 33.0\%$ $p > 0.05$). Most patients (81.3%) met their adult care providers before transition, but many patients were not meeting NICE recommendations for HbA1c targets of 48 mmol/mol (9.1% in paediatric care vs 6.3% in adult care).

Conclusion

Mean HbA1c and attendance rate does not vary significantly after transition to adult care and loss to follow-up was minimal, indicating that the current process is effective in maintaining similar treatment standards to pre-transfer. The audit shows that most patients do meet their adult care providers and highlights scope for improvement to achieve NICE guidelines for HbA1c monitoring.

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P27

The physical and psychological impact of the COVID-19 pandemic on children and young people with diabetes

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Background

During the pandemic, children and young people (CYP) have been in social isolation and faced many changes to their normal routine. Limited research has been done to understand how CYP with diabetes have been affected.

Objective

The objective of this study was to understand how CYP with diabetes have been affected by the COVID-19 pandemic.

Methods

Questionnaires were produced which included both quantitative and qualitative questions. The questionnaires were then distributed to patients and their carers during the paediatric diabetes clinics held at CAVUHB between 30th March 2021 and 22nd April 2021. The questionnaires were also uploaded to the DigiBete platform and local online parent support groups.

Results

There were 54 responses to the questionnaires. Participants said that COVID-19 had the most significant impact on diabetes management, CYP's psychological wellbeing, and relationships with peers. On a score of one to five, one meaning COVID had no impact and five meaning COVID had a significant impact, psychological wellbeing scored an average of 3.53 by CYP and 2.95 by parents and carers. Diabetes management scored an average of 2.73 by CYP and 3.08 by parents and carers. Participants also believed the pandemic affected the ability to access diabetes related healthcare and relationships within their families. For few participants, this was a positive impact. Most participants said social isolation from family and friends had a negative impact on the wellbeing of children and young people. Being in lockdown resulted in a change in normal routine and less physical activity compared to pre-COVID times; both factors significantly affected patient's blood glucose measurements.

Conclusions

CYP with diabetes have been affected by the changes introduced during the COVID-19 pandemic, most commonly in a negative way. Management of their diabetes was more difficult as well as dealing with the negative affects social isolation had on CYP's wellbeing.

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P28

Diabetic Ketoacidosis with severe hypokalaemia and persistent hypernatremia in an adolescent girl with Covid-19

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Introduction

Diabetic ketoacidosis (DKA) remains a common presentation of type 1 diabetes (T1D) in children. During the COVID-19 pandemic, rates of presentation in DKA increased. Electrolyte abnormalities can occur during DKA treatment, but they are uncommon at presentation. We report a teenage girl with new-onset T1D presenting in severe DKA, complicated by profound hypokalaemia and hypernatremia.

Case Report

A previously healthy 13-year-old girl was admitted during the COVID-19 pandemic with 9-week history of polyuria, polydipsia, and weight loss. Initial laboratory findings showed: blood glucose 32 mmol/l, ketone 7 mmol/l, pH 7.06, bicarbonates 8.3 mmol/l; potassium 1.9 mmol/l, sodium 134 mmol/l. She showed severe dehydration, Kussmaul breathing and tachycardia (126 bpm); Glasgow coma scale (GCS) was initially 15. She also tested positive for Sars-Cov2, despite being asymptomatic. Following initial fluid management based on BSPED guidelines, potassium infusion was started via central line and rates increased to the maximum due to profound hypokalaemia (lowest value: 1.7 mmol/l), associated with runs of bradycardia (40-50 beats/min) and premature ventricular beats on ECG. Due to persistent hypokalaemia, intravenous insulin was delayed for 15 h, and started at a modified rate of 0.03 units/kg/h, once serum potassium was >2.5 mmol/l, and rates gradually increased in intensive care. Over the first 24 h, she remained acidotic, hypertensive and GCS dropped to 8. She was treated with hypertonic saline and mannitol due to suspicion of cerebral oedema. Over the next 24-32h, GCS gradually improved, and potassium levels normalised.

However, corrected sodium increased up to 172 mmol/l. Thus fluids were changed to 0.45% saline and free water through NG commenced. Acidosis, ketosis and blood glucose gradually normalised. The girl made full recovery without any neurological deficit and discharged after 5 days on a basal-bolus insulin regimen.

Conclusions

This case highlights the challenges associated with profound hypokalaemia at DKA presentation, requiring delaying and reducing insulin infusion rates. It also underscores the importance of judicious use of hypertonic saline fluid in management of suspected cerebral oedema, especially if sodium levels are on the rise. The severity of the DKA episode in this patient may have been precipitated by the concomitant COVID-19 infection.

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P29

Initial insulin dose and trend review for CYP with T1DM

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Introduction

Recommended starting insulin doses in CYP with newly diagnosed type 1 diabetes vary widely from 0.3 to 1.0 U/kg/day. However, there is no study for rate of change of insulin dose in first few months of initiating insulin.

Aim

Retrospective review of insulin total daily dose at diagnosis, hospital discharge, and at first clinic, documenting changes in % basal insulin with time, considering any impact of insulin treatment on body weight and HbA1c after diagnosis. Local policy advises a starting dose of 0.7 units/kg.

Method

Data for 77 CYP aged 1-16 with newly diagnosed type 1 diabetes were collected over a 4-year period from clinical notes, clinic letters, electronic patient records and diasend® (diabetes data analysis software). Trends of total daily doses of insulin, % basal insulin, ICR, ISF, body weight and HbA1c were reviewed.

Results

The mean age at onset of diagnosis was 10.6 years (range 1.6 to 15.9 years); 55% of male and 45% of female subjects were identified. The median duration from the date of hospital discharge to the time of review at first clinic was 48 days with average number of contacts of 3.4 times in between. 26 children (33.8%) presented with DKA at the time of diagnosis. Total daily dose of insulin decreased from average 0.78 units/kg/day to 0.62 within median 48 days of starting insulin. % Basal insulin increased from 42.7% to 48% along with ICR and ISF trends, indicating the rise of insulin requirement which correlates with the body weight of CYP increasing by 11.2% in the same period. HbA1c trend was reassuring with improvement from average 106.33 mmol/mol at diagnosis to 65.3 mmol/mol at first clinic.

Conclusion

Total daily dose of insulin per weight decreased in first 1-2 months with no significant rise in between discharge and first clinic; the basal percentage remained in the recommended range of 40-50%. The unit initial starting dose seems appropriate.

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P30

New protocol DKA Audit 2020

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Background

- Updated guidance on management of DKA in 2020.
- Main changes:
  - Diagnostic Criteria
    - *same ketone/pH criteria but serum bicarbonate level lower (<15 mmol/l)*
  - Severity:
    - *pH <7.3 or bicarb <15=Mild DKA*
      pH <7.2 or bicarb <10=Moderate DKA
      pH <7.1 or bicarb <5=Severe DKA
    - *previously pH >7.1 classified as "mild or moderate".*
  - Senior support - *Previously recommended to discuss now "Always consult with the consultant paediatrician"*
  - Resuscitation Fluids
    - *Shocked=20ml/kg over 15 mins*
    - *Two further 10ml/kg can be given (up to 40ml/kg).*
    - *Discussion with HDU as after 40ml/kg inotropes considered.*
  - Bolus Fluids
    - *Non-shocked DKA patients should get a 10ml/kg bolus over 60 mins*
    - *IV fluids are not always required. Oral rehydration with monitoring of ketone levels can be used.*
  - Maintenance Fluids-
    - *Traditional Holliday-Segar formula.*
    - *Grading severity=fluid deficit*
    - *Maximum weight of 80 kg/97th centile for age (whichever lower)*
  - Potassium Maintenance
    - *If hyperkalaemic no additional potassium until urine passed or potassium back to normal.*
  - Insulin
    - *Consider long-acting subcutaneous insulin.*
  - Protocol used:
    - *Manage age 16-17 according to the guidelines for the teams they are under*

Aims

- Primary
  - Review guidance 1 year on regarding adherence to BSPED protocol.
- Secondary
  - Compare with previous audit of length of stay of newly diagnosed.

Standards

- BSPED DKA Protocol 2020

Methods

- Admission notes reviewed 15/04/2020-15/04/2021.

Results

- Total number 17/28 in DKA.
- Bicarbonate range "incalculable"-18.9.
  - 94% <15.
- x8severe, x2moderate & x6mild DKA.
  - All graded appropriately.
- Initial potassium 3.3-5.1.
  - None needed consideration of when to add potassium to IV fluids.
- No 16-18yo admitted
- Consultant made aware of all admissions
- 100% appropriate bolus
- 100% appropriate IVF
  - One managed with subcutaneous insulin and oral fluids
- 100% appropriate IV insulin
- Average length of stay 7.18 days
  - Previous length of stay average 6.6 days
- 41% long-acting insulin started

Conclusion

- Good compliance/uptake of the new protocol.
- Slightly longer duration of stay.
- Some difficulties comparing to previous data as age of admission raised to 16.
- 17/28 newly diagnosed in DKA compared to 2017 audit 6/21 admissions. Not explained due to increase in age (1 patient >14y which was previous limit).

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P31

An analysis of hospital admissions of children with Type1 DM in a district hospital

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Background

Poor diabetes control is associated with increased risks in all types of hospital admission. Admission into hospital among children and young people with diabetes places a large burden on the NHS resources. For example the cost of a DKA stay per patient is £2064[1].

Introduction

We analysed the paediatric admissions to hospital of those in T1DM. Our objective was to compare our type of hospital admissions to the national paediatric diabetes audit.

Methodology

We retrospectively collected data from a manual review of case notes and read of electronic discharge letters between the period '1st April 2018 – 31st March 2019' [$n=61$] and from the '1st April 2019 – 31st March 2020' [$n=47$].

Results

In 2018-19 the east of England reported 20% of T1DM had DKA at diagnosis. In our hospital 42% [$n=16$] of our newly diagnosed T1DM had DKA at admission. This trend worsened in 2019-20 with east of England reporting 17.5% of T1DM having DKA at diagnosis, whilst our hospital had 53% [$n=10$].

Conclusion
The areas covered by our hospital have consistently significantly higher rates of admission of DKA at diagnosis in T1DM compared to the national average.
Discussion
On analysis of the data, GP's we noted ignorance in 37% [$n=14$] of cases in 2018-19 of new diagnosis T1DM. This was due to patient's families home testing, patient becoming too unwell and attending A&E or GP sending patient into a routine clinic as opposed to an urgent clinic. However despite there is clearly a lack of public awareness into the warning signs for diabetes in children. Key symptoms such as polyuria, polydipsia and weight loss should prompt an urgent blood sugar sampling which should prompt admission.Posters such as the 4T's made by Diabetes UK are already well disseminated however it may also be worth noting that a larger social media presence would be better utilised to target the younger population.
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Gonadal, DSD and Reproduction

P32

Using SITAR analysis to explore the impact of gonadotropin-releasing hormone analogues on the pubertal growth spurt in adolescents with gender dysphoria

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Gonadotropin-releasing hormone analogues (GnRHa) are prescribed to adolescents with gender dysphoria under age 15 who have reached Tanner stage 2/3 to prevent progression through puberty and allow them time to consider their gender identity. The possible effects of the therapy on the pubertal growth spurt are poorly understood. A height more congruent with their identified gender is desired by transgender individuals, thus it is crucial that they are fully informed of its potential impact when consenting to the therapy. SuperImposition by Translation and Rotation (SITAR) growth curve analysis was used to study the pubertal growth spurt in transgender individuals on GnRHa therapy. SITAR is a nonlinear mixed effects growth model that estimates the age at peak height velocity (APV) and peak height velocity (PHV) in individuals. This was a retrospective observational study using patient records. SITAR analysis was applied separately to groups of transboys ($n=35$) and transgirls ($n=34$). The growth of cis-gender females ($n=70$) and males ($n=54$) recorded during the longitudinal Chard Growth Study (Cole *et al*., 2015) was modelled and used for comparison. The majority of transboys presented post-menarche, in the later stages of their pubertal growth spurt, thus the impact of GnRHa therapy was minimal. In transgirls the APV was not delayed but the PHV was reduced resulting in less pubertal growth. Further growth after the pubertal spurt occurred in both groups, and in transboys it could be attributed to the initiation of cross-sex hormone therapy. This study offers evidence that GnRHa therapy may alter the dynamics of the pubertal growth spurt, particularly in transgirls so care needs to be exercised as to the timing of the treatments. Finally, an extended growth spurt is seen after age 16 years, concomitant with the starting of cross sex hormone treatment which may have an enhancing effect on final height in transgender individuals.
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P33

Breast Satisfaction in adult women with Turner Syndrome – an international survey employing the BREAST-Q questionnaire

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Context
Turner syndrome (TS) is associated with short stature, delayed puberty, primary ovarian insufficiency, infertility, and other features. The majority of girls with TS require pubertal induction and life-long oestrogen replacement therapy. There is paucity of data in adult TS on the efficacy of pubertal induction, such as breast satisfaction. Patient-related outcome measures (PROMs) assess the quality of care and treatment from the patient's perspective. We have employed the BREAST-Q questionnaire, a validated and widely used PROM to assess outcomes of breast surgery, to explore breast satisfaction in Turner women.
Design
International survey on self-reported PROM (Breast-Q) in Turner Women matched to a control dataset.
Methods
We confirmed the suitability of the BREAST-Q pre-augmentation module for the study population through qualitative interviews. An online questionnaire was created, containing the four domains of the BREAST-Q pre-augmentation module, demographics and health history. The survey was online advertised through TS support groups (03-10/2018). Adult Turner women (age 18-45 years) were eligible. BREAST-Q scores were matched to normative data obtained from the Army of Women (AOW), an online community of healthy volunteers from the US.
Results
Eighty-three valid responses were received. Median age was 38 years (range: 18-45 years) and the majority ($n=81$; 99%) were White Caucasian. Median age at menarche was 15.5 years, and $n=72$ (88%) received pubertal induction therapy as teenagers. To evaluate BREAST-Q scores compared to controls, we were able to match $n=71$ Turner women to one control for age, BMI and level of education. We found significantly lower BREAST-Q scores in Turner women for the domains 'Satisfaction with Breast' ($P=0.021$), 'Psychosocial Wellbeing' ($P<0.0001$) and 'Sexual Wellbeing' ($P<0.0001$), but not for 'Physical Wellbeing' ($P=0.52$); Turner women who had received oestrogen replacement therapy reported lower control-adjusted delta scores for the same domains compared to Turner women who had not received oestrogen therapy ($n=63$ vs. 8; $P<0.0001$) . There were no differences in other TS subgroups (age at menarche, BMI, karyotype and age at diagnosis).
Conclusions
We report patient-related outcome measures assessing breast satisfaction in women with TS and observe lower self-reported breast satisfaction in adult Turner women.
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P34

Characteristics of 46,XY complete and partial gonadal dysgenesis- A pilot study

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Gonadal dysgenesis (GD) is characterised by maldevelopment of the gonads and is classified as complete (CGD) or partial (PGD) depending on gonadal morphology and function. The phenotype of PGD is variable and diagnosis is based on clinical and biochemical features, coupled with gonadal histology and genetic findings. "46,XY Gonadal Dysgenesis: diagnosis and long-term outcome" has recently been approved as an I-DSD Registry-based study. The aim is to characterise the phenotype of PGD and their pubertal development comparing with CGD. We have analysed our cohort of patients as a pilot study.
Methods
Inclusion criteria for PGD: (1) 46XY karyotype, (2) atypical genitalia, (3) at least of one of the following: (A) clinical evidence of testis dysgenesis (T level after HCG < double the basal T value, low AMH or inhibin B or Mullerian derivatives present), (B) histology consistent with dysgenesis, or (C) known gene variants associated with GD. A CGD group was analysed as a comparator.
Results
CGD, $n=24$; PGD assigned female, $n=13$; PGD assigned male, $n=7$. In CGD, 44% ($n=8/18$) presented with primary amenorrhoea, the remainder presenting

earlier with, for example, an abdominal mass, inguinal hernia or a serendipitous XY karyotype. Those with PGD presented early with atypical genitalia. Mean external masculinisation scores (EMS) for CGD, PGD female and PGD male were 1.2, 3.4, and 5.3, respectively. A uterus was frequently identified (CGD, 78%; PGD assigned female, 55%; PGD assigned male, 40%). Genetic confirmation was infrequent: CGD (SRY, $n=4$; NR5A1, $n=3$) and only one PGD (male-assigned, SRY). 50% ($n=3/6$) of PGD assigned male showed testosterone response to hCG, despite histology consistent with dysgenesis, which is in contrast to PGD assigned female, with 14% ($n=1/7$) showing testosterone response.
Conclusions
This pilot study confirms heterogeneity in the collective features of PGD vs CGD. A high prevalence of uterine remnants is a simple phenotypic marker of testis dysfunction. Further studies are required to correlate this finding with definitive histology of dysgenesis. In turn, outcome studies are sparse. The I-DSD based collaborative study offers the opportunity to rectify these shortcomings.

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P35

Two brothers with rare NROB1 mutation presenting with dichotomus pubertal presentations

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Background and Purpose
AHC (X-linked adrenal hypoplasia congenita) is a rare cause of adrenal insufficiency due to mutations in NROB1 gene. It traditionally causes hypogonadotropic hypogonadism. Rare cases of central precocious puberty due to NROB1 mutation has been reported so far. We present two interesting cases of NROB1 mutation from a same family with different presentations. This is first case report of NROB1 mutation from Pakistan.
Case Report
Index case boy presented at 15 day of life with adrenal crises and was treated with hydrocortisone and florinef which was subsequently continued. Later, at 11 month of age he developed precocious puberty with tanner staging III, bilateral testicular volume was 6 ml, penile length of 5 cm and dark pigmented genitalia. Investigations revealed low Na and high K, high ACTH, high Renin, increase LH, FSH, & Testosterone. His short Synacthen test with 17 OHP was normal while he showed advanced bone age. Genetic mutation revealed NROB1 mutation hemizygous (variant c.327C > A(p.Cys109). He was then treated with a GnRH agonist along with steroid replacement therapy. On follow up after 6 months of treatment his testicular volume remained unchanged where as pubic hair slightly reduced. Interestingly his elder brother who is now 15 ½ years old also presented at the age of 1 month with adrenal crises and treated as primary adrenal insufficiency, is showing arrested puberty with Tanner scoring III and bilateral testicular volume 6/6 for past 1 year. His genetic mutation also revealed same NROB1 hemizygous mutation.
Conclusion
Hypogonadotropic hypogonadism is classic feature of X-linked AHC but it can also manifest as normal puberty or in rare cases as precocious puberty so spectrum of NROB1 gene is very wide. Mechanism of precocious puberty is yet to be understood. Proposed theory suggest that possibly loss of one or more transcription factor which suppress puberty encoding gene.
Keywords
Hypogonadotropic hypogonadism, precocious puberty, adrenal insufficiency
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P36

Neuroblastoma with concurrent X chromosome monosomy, a coincidence or an association?

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Background
Turner's syndrome (TS) affects 25-50 per 100,000 females. Germinal cell tumour risk is described for TS with Y-chromosome presence (12%) and gonadal dysgenesis (15-35%) but other cancer risk is less well described. Neuroblastoma accounts for 6% of UK childhood cancer registrations, is the commonest cancer diagnosed in the first year of life and the most common extra-cranial solid tumour in childhood. It carries a UK incidence of 10.9 cases/million children. Previous literature suggests that X-chromosome monosomy confers an increased risk of solid tumour formation and could be associated with neural crest derived tumours.
Case Descriptions
Case 1 presented at 10 days of age with genital ambiguity. There was penoscrotal hypospadias and bilateral undescended testes with left gonad palpable in the groin (EMS score 4). Early ultrasound suggested no internal Mullerian structures, hCG test showed a good testosterone response and Karyotype (5/30) 45XO/46,XY (25/30). He was assigned male sex of rearing. He later presented with an incarcerated inguinal hernia at 6 months of age. At hernia repair, internal Mullerian structures were noted and left gonad had ovarian appearance. MRI for further DSD assessment revealed a left supra-renal mass which was histologically identified as a localised differentiating neuroblastoma and staging stratified as intermediate risk. The neuroblastoma was incompletely excised by laparoscopic excision biopsy, and he commenced treatment with chemotherapy. Case 2 presented at 3 years. An abdominal ultrasound carried out for spasmodic abdominal pain with associated autonomic symptoms showed an adrenal/paraspinal mass. Undifferentiated neuroblastoma was histologically confirmed, staging stratified as intermediate/high risk. She received treatment with chemotherapy, surgery, radiotherapy and immunotherapy. She was noted to have short stature on initial presentation with height SDS -2.76. Her expected target height is between 25th- 50th percentile. Workup for the neuroblastoma revealed a horseshoe kidney and a small PDA. Cytogenetic analysis later confirmed a diagnosis of TS (45,XO).
Discussion
Our cases add to support previous literature highlighting a possible link between X-chromosome monosomy and neuroblastoma. Clinicians should have a high index of suspicion to aid early identification and treatment outcome. Further research is required to better quantify this association.

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P37

Primary hypogonadism: better not just think of klinefelter!

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Background
Klinefelter syndrome is the most common sex chromosome abnormality causing primary hypogonadism and affects approximately 1 to 2.5 per 1000 males. However, other rarer sex chromosomal abnormalities have been associated to testicular dysfunction.
Clinical Case
A thirteen-year-old male was referenced to Pediatric consultation due to obesity starting around age four. Perinatal background: maternal gestational diabetes controlled with diet and 10-kilogram weight gain; caesarean delivery at 40 gestational weeks; Apgar score 4/10 (needed oxygen therapy and initial inflations); birth weight 4580 grams (+2.27 ZS); hypoglycemia neonatal episode. Breastfeeding up to 2.5 years. Clinic background: Some symptomatic episodes of fasting and postprandial hypoglycemia, ENT surgery at 7 years old due to conductive hearing loss and learning difficulties, attention deficit, progressive social problems and opposition behavior, culminating in sexual disinhibition and substance abuse. He was medicated with metilphenidate and topiramate. Family history: maternal obesity submitted to bariatric surgery and father with arterial hypertension and dyslipidemia.Several eating errors were evident. He used to play hockey three times a week. Daily screen time was less than 1 hour. At physical examination, weight: 117.6 kg, height: 182 cm (+3.18 ZS), Body Mass Index: 35.5 kg/m^2 (+3.48 ZS), blood pressure: 136/58 mmHg (P90/<P5), heart rate: 76 bpm; prognathism and bilateral eyelid ptosis, cervical and axillary acanthosis nigricans, abdominal stretch marks; normal male external genitalia; testicular volume: 12 mL (right) and 15 mL (left); Tanner pubertal stage: G3P5. Complementary investigation: normal lipidogram; glycated hemoglobin: 5.0%; insulin: 16.3 mUI/mL (<30); FSH: 21.4 mUI/mL (0.4-8.7), LH: 8.6 mUI/mL (0.5-5.3), total testosterone: 335.2 ng/dL (15-500), cortisol: 13.9 ug/dL (<23) and normal thyroid function. Normal abdominal and testicular ultrasounds. Chromosome microarray identified a structural rearrangement in Y chromosome and karyotype evidenced a dicentric Y chromosome with impact on spermatogenesis (46X,Yidic(Y)(q11.2)). Whole Exome Sequencing was inconclusive.
Conclusion
This clinical case discloses the importance of carefully integrating all background information with clinical evolution. Furthermore, it highlights the role of genetics not only for sex chromosome abnormalities identification, but also for a better

understanding of the patient's syndromic presentation, as well as management of future prevention.

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Late Effects of Cancer Treatment

P38

Timing of growth hormone initiation is not associated with brain tumour progression

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Introduction
Several publications now demonstrate that growth hormone therapy in replacement doses does not increase the future risk of recurrence in brain tumours. However, there is less certainty about the best and safest time to start growth hormone (GH) therapy after completion of primary treatment with recent guidance suggesting that a delay of 1 year is appropriate. We plan to determine if the timing of GH initiation is related to the likelihood of tumour progression.
Method
We retrospectively reviewed data of 50 children currently on GH replacement therapy as a result of brain tumours after completion of primary treatment at a large tertiary paediatric endocrinology centre.
Results
22 patients were male. The median age was 12.4 years (IQR 10.6 to 14.6) at last follow-up and median age at tumour diagnosis was 5.1 years (IQR 1.1 to 8.05). The most common diagnoses were craniopharyngioma (24%), low grade glioma (20%), medulloblastoma (14%), and germinoma (10%). One patient had a tumour predisposition syndrome (MEN1). 78% had primary surgical treatment, 62% received chemotherapy and 58% radiotherapy. Other endocrine deficits included TSH (32%), ACTH (18%) and LH/FSH (10%) deficiencies, posterior pituitary dysfunction (15%), and central precocious puberty (7%). The median time from end of treatment for diagnosis of GH was 0.83 years (IQR 0.04 to 3.04) with a height SDS at diagnosis of -1.22 (IQR -1.93 to -0.38). Median time of GH initiation after end of treatment (EOT) was 1.65 years (range 0.02 to 11.0). Only 9 progressed after starting GH, with a median time of GH initiation after EOT of 0.79 years (range 0.15 to 9.3) vs 1.73 years (range 0.02 to 11.0) in those who did not progress ($P=0.96$).
Conclusions
This analysis demonstrates no significant association of the timing of GH therapy in relation to the EOT and tumour progression. GH replacement can therefore be started as early as possible (even <1 year from EOT) in patients with brain tumours regardless of histology to maximise adult height and improve long-term bone density.

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Learning from Mistakes

P39

'When you have eliminated the impossible, whatever remains, however improbable, must be the truth?'

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Background
Hypoglycaemia is a common presentation in paediatrics, linked to rare endocrine pathologies. This case highlights potential pitfalls when assessing and managing a child with hypoglycaemia.
Presenting problem
A 15-year-old, previously well female, presented with significant hypoglycaemia (2.2 mmol/l). A hypoglycaemia screen was performed which revealed an inappropriately low cortisol (111nmol/l), she was therefore treated for adrenal insufficiency. Despite this, the hypoglycaemia persisted. She had recurrent episodes (1.3-2.8 mmol/l) on maintenance hydrocortisone, stress dosing, in the absence of intercurrent illness or stress and in spite of an intravenous dextrose infusion. There was a family history of maternal diabetes, reported to be taking metformin. The patient was not on regular medication, over the counter medicine or herbal remedies and her psychosocial screening was unremarkable.
Clinical management
Further investigations included early morning cortisol (96nmol/l) and baseline cortisol on synacthen test <50nmol/l. Adrenal antibodies and ACTH were pending at this time. There was a one-month delay in receiving the initial hypoglycaemia screen insulin levels (due to delays associated with referal laboratory send away); insulin 308pmol/l and c-peptide 1540pmol/l. The endogenous insulin production raised concerns of an insulinoma. The patient was commenced on diazoxide at 7 mg/kg/day and underwent pancreatic imaging (ultrasound and MRI) which were unremarkable. Further imaging modalities were being considered, including octreotide scintigrophy, when her urine toxicology results were reported, revealing gliclazide (sulphonylurea) abuse. This was cross referenced with her mother's GP records, with her mother's consent. The patient successfully discontinued hydrocortisone and diazoxide. She was discharged with psychological support.
Discussion
This case highlights the role of counter-regulation and habituation in the context of hypoglycaemia, which need to be taken into account when interpreting results. It demonstrates value in considering urine toxicology early in teenagers presenting with hypoglycaemia. Ketones were not performed on the first hypoglycaemia screen and this simple bedside test holds great value in narrowing differentials. Of note diazoxide can be used as an effective treatment for sulphonylrea overdose. Whilst in this case there was some evidence of rare endocrine pathology, intentional overdose is far more common, as is medication non-compliance; clinicians should keep an open mind.

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Miscellaneous

P40

Can playing a computer game assess muscle function? Using ability captured through interactive video evaluation (ACTIVE) in duchenne muscular dystrophy

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Introduction
Duchenne muscular dystrophy (DMD) is associated with progressive decline in muscle function and loss of ambulation in the teenage years. Objective assessments of upper limb performance are required but functional assessments and magnetic resonance imaging (MRI) are time consuming and costly. ACTIVE-seated (Ability Captured Through Interactive Video Evaluation) is a fun, inexpensive, movement tracking video game that can measure Functional Reaching Volume (FRV).
Aim
To establish whether data obtained using ACTIVE-seated are comparable to measures of muscle performance and pathology using functional assessment and MRI.
Methods
Data were obtained from 15 adolescent boys with DMD on 3 occasions (clinical trial NCT02571205). ACTIVE-seated output (FRV - lower, middle and upper) was compared with Performance of Upper Limb 2.0 (PUL), Brooke Upper Extremity Scale, myometry and MRI (arm fat fraction, using 3-point Dixon and T2 relaxation).
Results
Data at 1 year were analysed. ACTIVE-seated correlated with Brooke score ($P=0.0275$) and was related to whole arm PUL values ($r=0.941, P<0.0005$), fat fraction ($r=-0.6923, P=0.01226$) and contractile cross-sectional area ($r=0.5769, P=0.0390$). Lower FRV had close associations with grip myometry ($r=1.7909, P=0.0037$). Upper FRV correlated closely with shoulder PUL ($r=0.89713, P<0.0005$) and shoulder abduction myometry ($r=0.7063, P=0.0102$). There was no association with T2 relaxation time ($P=0.5879$) which acted as a control in this context.
Conclusion
The close relationship between ACTIVE-seated data and traditional functional assessments as well as quantitative arm muscle MRI suggests that it may be a useful addition to existing assessment tools.

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P41

Paediatric society calls for a review of access to funding for continuous glucose monitoring systems for patients with recurrent hypoglycaemia

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Continuous glucose monitoring (CGM) allows continuous real-time blood glucose monitoring and informs users of blood glucose trend data and alarms which warn users of high or low blood glucose readings. Current evidence suggests that CGM can reduce episodes of hypoglycaemia in conditions such as congenital hyperinsulinism and metabolic disorders. Hypoglycaemia secondary to these conditions is serious with almost 50% of children demonstrating neurological impairments as a result of recurrent hypoglycaemic events. The current standard of care for these patients are frequent observations and intermittent fingerpick testing. However, this provides no details of trends with no alarm settings and carers risks missing hypoglycaemia between infrequent tests. CGM devices are currently only recommended by the National Institute of Clinical Excellence (NICE) for patients with Type 1 diabetes as most studies have targeted a reduction in HbA1C rather than hypoglycaemia episodes as a clinical end point. While there is clear guidance from NICE for patients with diabetes with regards to whom CGM should be prescribed, funding pathways for CGM are complex. Access has been reported to be highly variable determined locally by Clinical Commissioning Groups (CCGs), some require individual funding applications (IFAs) whereas others have local policies on who should access CGM devices[4]. The British Society of Paediatric Endocrinology and Diabetes (BSPED) conducted a national survey in England, Wales, Scotland and Northern Ireland between 1st January to 30th February 2021 which included all of the 22-specialist paediatric endocrine centres. The results of the national survey found that a significant proportion of teams were struggling to access funding for CGM, and funding streams were highly variable leading to health inequalities.BSPED urges for a national mandate for CGM access to be considered as a priority to address such inequalities that currently exclude patients without the diagnosis of diabetes from accessing CGM easily. BSPED request that the scope and funding for CGM be widened to include patients without diabetes who suffer from severe and recurrent hypoglycaemia.

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P42

A rare case of steroid cell tumor, not otherwise specified (NOS) of the ovary presenting with cushing syndrome and hyperandrogenism

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Background
Steroid cell tumour of ovaries comes under sex cord stromal tumour that accounts less than 0.1% of all ovarian tumour. Majority are benign in childhood age group. It may produce steroids and testosterone resulting in virilisation and Cushing's syndrome. Histology remains the gold standard for diagnosis of NOS. The gross appearance of NOS generally is well circumscribed, solid and noncalcifed with a lobulated appearance Till date only 10 cases has been reported in pubmed-search of steroid cell ovarian tumour NOS in childhood age group and this is first case report in Pakistan. We have also reviewed the literature on the epidemiology, clinical presentations, imaging and histological findings, and the treatment options on this disease presenting in prepubertal age group.
Case report
We present a 6 year old Pakistani girl who presented to us with complains of weight gain and hirsutism for past 10 months. On examination she had obvious cushingoid facies, facial hair growth, hypertrichosis, buffalo hump, acanthosis nigracans and marked hirsutism (ferriman Gallwey score of 25). Her blood pressure was >99th centile whereas tanner staging was P3 A1 B1. Investigation showed increased level of cortisol and loss of diurnal rhythm, increased testosterone levels and undetectable ACTH. B HCG and alpha fetoprotein levels were normal. Radiological it was a left adnexal mass of 6.9*8.1*4.9 cm (CC*TS*AP) measurement. She underwent left oophorectomy with findings of intact capsule and dilated vessels. Histopathological report revealed steroid cell tumour NOS (Not Otherwise specified) which was negative for malignancy. She was kept on intravenous hydrocortisone pre and post operative day to avoid adrenal crises. Postoperatively her levels of cortisol and testosterone became normal.
Conclusion
Steroid cell tumour NOS is a rare tumour which can be onerous to diagnose. Although rare, Steroid cell tumour of ovary should be considered in cases of childhood virilization. The typical clinical, radiological and histopathological findings can clinch the diagnosis in most of the cases however in difficult cases, immunohistochemistry can be useful.
Keywords
Steroid cell tumor, cushing syndrome, hyperandrogenism
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P43

Hypoglycaemia in paediatrics – Re-Audit post introduction of "Hypo Packs"

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Introduction
Hypoglycaemia is a common paediatric medical emergency, hence prompt treatment with appropriate investigations of causes is essential.
Aims
1) Re-audit investigations sent for children with hypoglycaemia after introduction of "Hypo-packs" from previous audit; (2) To improve awareness of local guidelines to unify clinical practice; (3) Review "Hypo-packs" and consider other improvements.
Methods
A retrospective audit of investigations taken in hypoglycaemic patients over 20 months using clinical notes after the introduction of hypoglycaemia packs to assess completion of hypoglycaemia screens.
Results
Over a 20-month period (May 2018–Dec 2019), 30 patients were coded as hypoglycaemic. Demographics: 19/30 = Female; Average age = 4.5 years (1 month–14 years); 14 were excluded (8 known diabetic patients, 1 known metabolic condition, 4 no documented hypoglycaemia, 1 referral with no hypoglycaemia in department). Of 16 remaining children - 7/16 had blood glucose < 2.6 at/during admission; 5/7 had a hypoglycaemia screen. 0/7 patients had complete investigations as per our local guidelines. Most commonly forgotten tests were 3-betahydroxybutrate and ketones. Final diagnoses included: 3/7 gastroenteritis, 1/7 refusal to eat, 1/7 viral infection with vomiting, 1/7 unknown diagnosis (BM 2.1), 1/7 adrenal insufficiency.
Conclusions
Despite the introduction of "Hypo packs", 0% of our patients had complete hypoglycaemia screens performed. The team felt that although the packs were useful they were difficult to find, not re-filled and not clear enough.
Changes made after re-audit:

- Hypoglycaemia lanyard cards have been given paediatric trainees to attach to their access badges/smart cards.
- "Hypo packs" changed to more clearly show which tests and which blood bottles are required (Table 1)
- Order sets being created on our online ordering system
- Responsibility of the last user of the "Hypo pack" to replenish

Table 1: Example of information table on ãHypo Packã and on lanyard cards

Test	Blood Bottles
Glucose	**1x Grey**
Insulin	
Free fatty acids	
3-beta Hydroxybutyrate	
Amino acids	
Carnitine profile	**3x Dark Green**
Cortisol	**2x Red**
Growth hormone	
Acyl-Carnitine	**Guthrie card (4 spots)**
ACTH	**1x Purple (EDTA)**
Ketones	**Ketone strip**
Lactate	**Gas**
Ammonia	**1x Purple EDTA (on ice)**
Urine organic acids	
Urine reducing substances	**2x urine pots**

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P44

Interpretation of CGM-measured nocturnal hypoglycaemia in congenital hyperinsulinism

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Background
Congenital Hyperinsulinism (CHI) is characterised by dysregulated and excess secretion of insulin leading to severe hypoglycaemia. Monitoring of glucose levels is essential in this condition as prolonged hypoglycaemia can cause life-threatening complications such as permanent neurological impairment. Interstitial glucose monitoring by continuous glucose monitoring (CGM) devices can identify nocturnal hypoglycaemia retrospectively through data analysis. Analysis can be conducted quickly using bespoke computer code, however this technique requires significant work initially to develop the code. We have aimed to investigate if manual methods are equivalent in the interpretation of nocturnal hypoglycaemia by CGM.
Methodology
Nocturnal CGM (00-0700 h) was investigated by two different glucose thresholds (<3.0 and <3.5 mmol/l) and two different criteria for an "episode" of hypoglycaemia using both coding (Python) and manual (visualisation of spreadsheet) methods in 23 patients (9395 data points) with CHI. Hypoglycaemia interpretations were compared to markers of disease severity.
Results
Hypoglycaemia interpretations were consistent between coding and manual methods. Mean percentage time in hypoglycaemia was similar by coding and manual methods for a threshold of 3.5 mmol/l [Criteria One (5% vs 4.9%, chi-square $=0.707$, $p=0.4$), Criteria Two (5.5% vs 4.7%, chi-square $=0.759$, $p=0.3$)] and a threshold of 3.0 mmol/l [Criteria One (1.05% vs 0.9%, chi-square $=0.817$, $p=0.4$), Criteria Two (0.95% vs 0.8%, chi-square $=0.721$, $p=0.4$)]. In univariate analysis of variance age or severity markers (pancreatic surgery/genetic mutations) did not predict percentage time spent hypoglycaemic (P all > 0.2).
Conclusion
Manual methods are equivalent to coding methods in the interpretation of nocturnal hypoglycaemia demonstrating this method's utility in routine clinical practice. Severity markers for CHI did not predict individual time spent hypoglycaemic, highlighting the importance of personalised CGM analysis in the management of hypoglycaemia due to CHI.

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P45

Heterozygous mutations in ATP-sensitive potassium channel (K_{ATP}) genes associated with transient and mild hyperinsulinaemic hypoglycaemia

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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 during the neonatal period and early childhood. Mutations in $K_{AT}P$ genes (*ABCC8* and *KCNJ11*), together account for up to 70% of CHI. CHI can either be transient or persistent. Transient CHI tends to resolve spontaneously and is not generally associated with genetic mutations. We present two cases with: [1] transient CHI & [2] mild (and potentially transient) CHI, associated with heterozygous mutations in *ABCC8* and *KCNJ11* respectively.
Cases
1. A term infant (birth weight: 3.2 kg), with no risk factors for hypoglycaemia, presented with seizures associated with a blood glucose (BG):0.5 mmol/l on day 2 of life. The investigations confirmed CHI, which was fully responsive to low dose of diazoxide (3 mg/kg/day). At 18 months, a 12 hour fast off diazoxide showed normoglycaemia with supressed insulin and appropriate increase in the ketone bodies indicating the resolution of CHI. The genetic testing showed a novel *ABCC8* variant (c.2476C>A). The parental testing is underway.
2. A term infant (birth weight: 4.3 kg), with no risk factors for hypoglycaemia, presented on day 3 of life with seizures, associated with a BG: <0.2 mmol/l. Subsequent investigations confirmed CHI, which was completely responsive to diazoxide (5 mg/kg/day). Genetic testing identified a maternally-inherited *KCNJ11* loss-of-function missense variant (p.Gly40Asp) of uncertain significance, as the mother appears clinically unaffected and did not have gestational diabetes. BG levels for the child are currently stable (>3.5 mmol/l) at 1 year of age at a diazoxide dose of 3 mg/kg/day. A controlled fast off diazoxide is awaited.

Discussion
Genetic testing is not normally indicated for transient CHI, but potentially should be considered if there are no associated risk factors. Although the clinical significance of $K_{AT}P$ mutations is currently unclear in the above two patients, it may have implications for postnatal BG monitoring in subsequent pregnancies, particularly due to the risk of neonatal hypoglycaemia and neurodevelopmental sequelae. Due to the associated gene locus, they may also have a predisposition to develop diabetes in later life, implying the need for long-term monitoring.

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Obesity

P46

Liraglutide with lifestyle modifications causing rapid weight loss in an adolescent with morbid obesity and life threatening sleep apnoea

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Introduction
The management of childhood obesity is complex and requires intensive input from a multidisciplinary team. Pharmaceutical interventions may be required in addition to lifestyle modifications to treat morbid obesity. In a double blind randomised controlled trial, liraglutide, a glucagon-like peptide 1 (GLP-1) agonist along with dietary and lifestyle interventions showed beneficial BMI reduction in children and adolescents. We present a morbidly obese adolescent with life threating obstructive hypoventilation who had a dramatic weight loss of 45.3 kg in a 12 month period following treatment with liraglutide.
Case
A 15year old boy with morbid obesity, 184.5 kg (BMI 56.6 kg/m^2, (SDS $+3.23$) presented with symptoms of severe sleep apnoea. The sleep study showed average oxygen saturation of 87% with an oxygen desaturation index of 56.4 consistent with significant obstructive sleep apnoea. He was established on non-invasive ventilator support [overnight continuous positive airway pressure] and was referred to the obesity team. The clinical history was not suggestive of an underlying monogenic cause of obesity. His clinical examination showed generalised obesity, without dysmorphism, signs of insulin resistance or cushingoid features. His investigations showed normal HbA1C (36 mmol/mol), liver function, thyroid function and oral glucose tolerance test. An echo cardiogram showed no evidence of pulmonary hypertension. A Calorie restricted diet (1800 kcal/day) was advised along with goal setting exercise. He was commenced on orlistat but stopped due to side effects. He was referred for bariatric surgery. Liraglutide was commenced in order to buy time before the bariatric surgery. He was commenced at a dose of 0.6 mg which was increased to 1.8 mg over a 12 month period. A further increase in the dose (maximum recommended dose 3.0 mg) was withheld due to the gastrointestinal side effects. A significant reduction of weight from 183.5 kg to 139.2 kg was observed in a 12month period with a 25% reduction in BMI from 56.6 kg/m^2 (SDS $+3.23$) to 42.5 kg/m^2(SDS $+2.87$) and a reduction in BMI SDS score of -0.36.
Conclusion
Evidence from clinical trials supports the use of liraglutide in adolescents with severe obesity and should be considered as a potential treatment option, especially in motivated adolescents.

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P47

Evaluating a tertiary paediatric multidisciplinary weight management service

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Introduction
The Tier 3 paediatric weight management service at University Hospital Southampton comprises a Paediatric Endocrine Consultant, a Clinical Nurse Specialist and Specialist Dieticians. Children may be referred if they have an endocrinopathy, metabolic co-morbidity or obesity syndrome. We offer at least two years of engagement within the service prior to discharge.
Service Evaluation
Twenty-six Tier 3 patients were under follow-up between 1st January 2018 and 1st April 2020. The median age at first appointment was 9.8 years (1.7 – 17.2 years), with 54% of patients male and 23% of Asian ethnicity. The average BMI SDS at the first appointment was 3.7. In terms of background, 27% had learning difficulties, ASD or ADHD or CAMHS involvement, 23% had hyperphagia, 19% had underlying chronic disease including kidney disease, airways disease and cancer and 15% had a genetic cause of obesity including T21, MC4R mutation and Bardet-Biedl Syndrome. In terms of co-morbidities, 46% were diagnosed with insulin resistance, 35% with obstructive sleep apnoea, 31% with non-alcoholic fatty liver disease, 19% with dyslipidaemia, 8% with polycystic ovarian syndrome and 4% with pre-diabetes (impaired fasting glycaemia or impaired glucose tolerance). A family history of high BMI, Gestational Diabetes Mellitus or Type 2 Diabetes Mellitus was common (52%). Seven patients (27%) received social services support. Eight patients (31%) received metformin and five patients (19%) were admitted for weight management. Of those discharged due to poor engagement, the average change in BMI SDS was -0.4. Of those remaining under follow-up, the average change in BMI SDS was -0.8. There were three to four MDT contacts per patient per year. The overall was not brought (WNB) rate was 15%.
Discussion
This service evaluation demonstrates: 1) these patients have complex health and social needs, with a high incidence of obesity-related co-morbidity, CAMHS and social services involvement and family weight/metabolic problems. 2) BMI improved by an average of 0.4 – 0.8 SDS under the current service structure, a metabolically meaningful improvement. 3) Patients are receiving significant specialist input every year, yet the overall WNB rate is high, highlighting the pressing need to work on patient and family engagement.

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P48

The role of paediatric doctors in addressing childhood obesity. What do parents think?

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Background
Nearly 1 in 3 of UK children are overweight or have obesity. Obesity is associated with a higher risk of physical, psychological, and social ill-health yet doctors often do not initiate a conversation with parents about weight when a child has obesity. Studies have shown that doctors frequently fail to address childhood obesity with families in general paediatric outpatient clinics. Doctors report fear of upsetting parents. Parental views on this are largely unexplored. A quality improvement project in our district general hospital was used to improve our response to childhood obesity. This QI project included a parental survey to inform service development.
Methods
Questionnaires were offered to the parents of 120 aged 2-16 years children attending face-to-face paediatric outpatient clinics in our hospital over a 5-day period. Questionnaires comprised of 4 closed Yes/No questions. Questionnaires were anonymous, separate from the clinic appointment and administered by reception staff. Parents were informed that participation was entirely voluntary.
Results
103 of parents completed the questionnaire (return rate: 86%). 97% of parents ($n=100$) answered Yes when asked "Do you think it is useful to check the weight of your child when attending a paediatric outpatient appointment?" 96% of parents answered Yes ($n=99$) when asked "Do you think the doctor seeing your child in outpatient clinic should inform you if your child has obesity?" 93% of parents ($n=96$) answered Yes when asked "Would you like the doctor to give dietary and lifestyle advice if your child had obesity?" 93% of parents ($n=96$) answered Yes when asked "Do you believe that healthcare professionals should receive training to have conversations about a child's weight with parents?"
Discussion
Doctors worry about causing distress when raising the issue of obesity but in contrast parents report that they want to be informed if their child has obesity. Parental feedback shows that parents expect healthcare professionals to initiate conversations about weight if a child has obesity and provide dietary and physical activity advice. There is a need to utilise this parental feedback and improve our clinical practice to play our role as paediatricians in addressing the obesity epidemic.

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P49

Plasma glucose and gut hormone responses in obese children after variable resistant starch and protein content

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Introduction
Resistant starch (RS) has beneficial effects on postprandial glucose metabolism in both animals and adults. Hitherto, it has not been studied in children. The long-term effects of RS in reducing obesity and improving metabolic profiles need to be investigated in children.
Objectives
Our objective was to compare serial plasma glucose, insulin, gut hormone profiles and satiety scores in obese children after meals, containing increasing amounts of RS.
Methods
This was a single blind, non-randomised, crossover study. 20 obese children, 10-13 years old and without comorbidities were recruited. Three test meals, (1) rice, (2) rice cooked with coconut oil and (3) rice with lentils, chosen for their increasing RS content, were given to all subjects in sequence after a 12-hour overnight fast. Between studies there was a one-week washout period. Blood samples were collected for glucose, insulin, leptin, glucagon like polypeptide (GLP) 1, ghrelin and PYY at 0, 60,120 and 180 minutes (at selected times for each analyte).
Results
There were 12 males and 8 females recruited to the study. Their median age (IQR) was 12 (10.8,12.5) years, and median BMI (IQR) was 26.2 kg/m^2 (23.6-27.85). Plasma glucose after meal 3 was significantly higher compared to after meals 2 and 1 respectively [C_{max} ($p=<0.05$) and AUC ($P=0.001$) in both]. Ghrelin after meal 3 was significantly lower compared to meals 1 and 2 (AUC, $P=0.004$). However, insulin, leptin, PYY and GLP1 were not significantly different between the three meals at 120 min and 180 mins. Median satiety scores were not significantly different between the three meals either.
Discussion
This study shows higher insulin AUC following meal 3 which contain RS and protein compared to meals 1 and 2 as expected. Meal 2 with RS alone has shown reduced insulin and blood glucose profile. There is a tendency to reduce satiety score in meal 3 however reduction in satiety score was not significantly different possibly due to small sample size. Gut hormones were not significantly affected by acutely taking RS in obese children. More frequent sampling and a higher RS content may have given different results and will be studied in a larger investigation.

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P50

BMI centiles for south asian children: do they need reconsideration?

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Introduction
Obese adults of South Asian origin in the UK are considered to be obese at a BMI of 27.5 kg/M^2 compared with 30 kg/m^2 for other groups and are at increased risk of obesity related disorders such as type 2 diabetes. From July 2021, GPs have been offered financial incentives for referral of adults to weight management services. However no provision or adjustments have been made for children and young people especially those of South Asian origin: this contrasts to the stated objectives for obesity management in the NHS Long term Plan. Is this lack of action increasing their lifelong risk of obesity related disorders?
Our Current State of Knowledge
Ideally a BMI centile 'action line' should be identified on the UK's paediatric BMI centile charts so that these children may be referred to specialised services. This 'action line' should relate to an outcome as is the case in adults for BMI values above 30 kg/M^2. The BMI centiles currently available for children were

not collected in an ethnicity specific way and it has been argued that they should not be used in such a way. However data from the National Child Measurement Programme, when adjusted from ethnicity specific measurements of body fat using deuterium dilution, provides supporting evidence that BMI underestimates body fat in overweight or obese South Asian children but not in most Black children. In addition there is evidence of reduced physical activity in South Asian London children and evidence of less parental concern about future overweight risk.

Conclusion

Evidence is accumulating that South Asian children are at particularly high risk of becoming overweight and developing obesity related problems in later life. While there is a relative lack of longitudinal obesity related outcome data for obese South Asian children, extrapolation from our knowledge of obesity outcomes in adults strongly support consideration of an action line adjustment to the equivalent of 27.5 mg/M^2 for South Asian children. This needs to be combined with good quality longitudinal outcome studies and a substantial improvement in obesity services for children and young people which are culturally relevant to that population.

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P51

Raised intracranial pressure – an under-recognised complication of childhood obesity

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Introduction

Raised intracranial pressure is a well-documented complication of obesity in the adult population, but this remains under-recognised in children and young people. The pathophysiology for this association remains unclear, but the complications of raised intracranial pressure can be devastating including potential visual loss. Therefore, the aim of our study was to investigate this link in children and young people.

Method

Retrospective data collection from individuals diagnosed with idiopathic intracranial hypertension (IIH) at a tertiary children's hospital over two years.

Results

18 patients were identified with a mean age at diagnosis of 11 years ($\pm$ 3.3SD; range: 6 to 15 years). 61% were female. The mean BMI was 30.3 kg/m^2 (range: 13.9 to 58.2 kg/m^2) and the mean BMI SDS was +2.5 (range: -1.24 to +4.46). 72.2% of individuals had BMI SDS $>$ 2. Headaches and eye signs (visual disturbances or ophthalmology findings) were the presenting symptoms and signs for 12 patients. 3 patients did not experience any symptoms and were found to have papilloedema on routine optician review. Diagnosis for all patients was via a lumbar puncture with 61% requiring theatre or admission to the radiology department for it to be successful. 82% of these required general anaesthetic. 83% of patients were treated medically and 11% required long-term neurosurgical interventions (ventriculoperitoneal and ventriculoatrial shunts). 6% did not require treatment.

Conclusion

These results show a clear association between IIH and obesity and highlight that being female may be a risk factor. IIH is not a well-recognised complication in paediatrics and therefore may not always be considered when health professionals review an individual with childhood obesity. Awareness to screen for IIH is essential so that permanent visual loss can be prevented.

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P52

A study on Complications associated with Childhood Obesity

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Introduction

Childhood obesity is a severe public health concern. Various complications are recognised in adults, but the data remains limited in the paediatric population. Therefore, the aim of this study is to investigate the complications observed in children and young people (CYP) with obesity.

Method

Retrospective data collection from 125 CYP aged between 0 and 18 years with a body mass index (BMI) standard deviation score (SDS) of two or more above the mean. Information for each patient regarding complications was analysed from the database.

Results

The mean age of the CYP was 10.9 years (SD$\pm$3.62, range: 2-18) with 65% of patients being female. The average BMI was 32.9 kg/m^2 (SD$\pm$6.6, range: 22.7-58.3) and average BMI SDS was +3.5 (SD$\pm$1.1, range: +2.06-+7.85). 47% and 33% of patients had 2 or more complications and at least one complication secondary to obesity, respectively. The most common complication was dyslipidaemia seen in 25% of individuals. This was followed by hypertension (18%) and mental health issues (18%), which included depression, anxiety and self-harm. 31% of patients had risk factors for type 2 diabetes mellitus (T2DM) [family history, acanthosis nigricans and/or insulin resistance]. Of those who had an oral glucose tolerance test (OGTT), 11.4% of the CYP were diagnosed with pre-diabetes and 9% with T2DM. Obstructive sleep apnoea and mobility issues were seen in 21% and 11% of individuals, retrospectively. Pubertal disorders were seen in 10% and 18% of individuals were diagnosed or had symptoms of polycystic ovary syndrome. Other complications include raised intracranial hypertension, non-alcoholic fatty liver disease, liver fibrosis, slipped upper femoral epiphysis, skin infections, nocturnal enuresis and gynaecomastia.

Conclusion

80% of the patients had at least one complication secondary to obesity. It is extremely important to carefully screen children and young people to identify these complications, so that interventions could be introduced as early as possible. The complications of childhood obesity may significantly impact the quality of life of those affected, and optimising weight loss support at an early stage could potentially improve the outcomes.

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Pituitary and Growth

P53

SGA, short stature, brachydactyly and joint stiffness due to SMAD4 variants in Myhre syndrome

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We present 3 children in a single centre with Myhre syndrome (MS) due to a heterozygous *SMAD4 Ile500val* mutation. Consistent features were brachydactyly, joint restriction, muscular hypertrophy, genital abnormalities, conductive hearing loss and developmental delay. SGA and height were variable. Diagnosis was made by next generation sequencing in patients 1 and 3 and on the skeletal survey in patient 2. Retrospectively, features of Myhre syndrome were present on the skeletal survey in all 3 patients, at young age.

Discussion

MS has been described in under 100 patients. MS is mostly caused by *SMAD4 Ile500Val* gain-of-function mutations(GOF) resulting in growth retardation and excessive fibrosis leading to keloid formation, cardiac fibrosis and tracheal stenosis after trauma/intervention. Making early diagnosis is important to avoid non-essential invasive procedures. *SMAD4* is the central intracellular mediator of TGF β and BMP signalling and inhibits chondrocyte differentiation and hypertrophy, and mice with *SMAD4* deletion in chondrocytes are dwarved. Gain-of-function leads to abnormal extracellular matrix formation, although the effect on growth plate chondrocytes is unclear. Neurosecretory dysfunction and variable response to GH has been described, in line with findings in patient 1. The mechanism for the neurosecretory dysfunction is not known.

Conclusion

MS may be more common than previously thought. SGA and height deficit are variable. GH treatment might increase height but can also accentuate muscular hypertropy. Skeletal surveys in our patients showed features at early age, and skeletal survey may therefore aid early diagnosis.

Clinical characteristics were as follows:

	Child 1	Child 2	Child 3
Clinical features			
Birth weight	-2.58 SDS	-2.00 SDS	-1.49 SDS
Current height	-2.75 SDS (14.3 years)	0.71 SDS (6.3 years)	-2.2 SDS (5.3 years)
Cardiac	-	-	VSD, PDA
Genitourinary	Cryptorchidism	Epispadias, megaprepuce	Undescended testis, inguinal hernia
Other		Keloid	
Investigations			
IGF-1 (Normal range)	23mcg/l (6-57.6), GH peak 6.7ng/mL	243mcg/l (18.1-307)	85 mcg/l (12-120), IGF-BP3 2.5 mg/l (0.5-2.9).
Skeletal survey	Brachydactyly, Prognathism (aged 4 years)	Large vertebral pedicles, Brachydactyly Prognathism (aged 5.5 years)	Large vertebral pedicles, Subtle brachydactyly, Prognathism (aged 6 months)
GH treatment	Yes, age 4–9.5 years, 77% increase in HV, stopped due to muscular hypertrophy	None	None

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P54

Short stature due to a WAC mutation in Desanto-Shinawi Syndrome

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We report a case of a girl with severe short stature (-3.5 SD) from the age of 2 years. She was born at term with a normal birth weight (-1.3 SD) to non-consanguineous Pakistani/British parents. She had global developmental delay, hypotonia and microcephaly (-2.0 SD). She also had juvenile xanthogranuloma, alternating esotropia, constipation and initial feeding difficulties. Her current height is -2.9 SD with a normal BMI, aged 11. Serum IGF1 at age 2 years was <25 (49-289 ng/ml), and was subsequently low or low-normal. Glucagon and primed insulin tolerance tests at age 6 and 11 years were normal (GH peaks 8.4 and 10.3 mcg/l). MRI brain and pituitary, karyotype, microarray and skeletal survey were normal. The Deciphering Developmental Disorders study reported a *WAC* (WW domain containing adapter with coil-coil) mutation on chromosome 10p12.1: (c.1298del heterozygote, p.(Ser433Leufs*8), resulting in a diagnosis of Desanto-Shinawi Syndrome (DESSH). This frameshift mutation has not been previously described. It is predicted to cause premature termination of the WAC protein and highly likely to be pathogenic. WAC pathogenic variants have been described throughout the gene. WAC is expressed in many tissues and expression in brain is highest in the caudate nucleus, substantia nigra and thalamus. WAC is involved in transcriptional regulation and meiosis, and increases mTOR activity. DESSH is a rare condition characterised by global developmental delay, behavioural problems, hypotonia, ocular and gastrointestinal abnormalities. Facial features of frontal bossing, flat nasal bridge and midfacial hypoplasia are common. Short stature is not usually reported as a main feature in DESSH; however, height was below -2 SD in approximately 30% of described cases and GHD has been reported in at least 2 patients. It is likely that the short stature in our case is related to the syndrome, and is associated with low IGF-1 concentration. In conclusion, we describe a new *WAC* variant leading to DESSH. We suggest that *WAC* variants may lead to short stature and that children with DESSH syndrome and short stature undergo endocrine evaluation. The role of WAC in growth and the GH-IGF1 axis deserves further research.

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P55

Duplication of pituitary gland-plus syndrome presenting with a transcranial nasal dermoid cyst

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Duplication of pituitary gland in association with other midline craniofacial anomalies -DPG-plus syndrome - is extremely rare. So far the only described endocrine associations are precocious or delayed puberty. We describe the multifaceted management of a female infant with DPG-plus syndrome. Interestingly, the patient also presented with trans-cranial nasal dermoid cyst and a nasal dimple with protruding hair, which hasn't been described in previously reported cases. Our patient was diagnosed with a cleft palate and an unusual tongue polyp after birth. She was hospitalised twice with respiratory distress, during feeding and in flat position, while awaiting assessment by a cleft surgeon. She was examined by the cleft surgeon at 11 weeks of age, who identified that her palatal cleft was unusually wide and that a large nasopharyngeal mass was partly filling the defect. He also noted that she had a nasal dermoid cyst, a nasal dimple with protruding hair, hypertelorism and low-set ears. The patient's MRI brain scan revealed duplicated pituitary gland, thickening of the floor of the third ventricle (hypothalamic hamartoma), basilar artery duplication, odontoid peg cleft, large right nasopharyngeal teratoma and trans-cranial nasal dermoid cyst extending through the nasal bones to just above the cribriform plate. A skull-base CT scan confirmed the midline cranial osseous defect. The patient was diagnosed with DPG-plus syndrome. Resection of nasopharyngeal mass and tongue polyp was performed at 8 months of age, which remarkably reduced the patient's breathing and feeding difficulties. Histopathology revealed the nasopharyngeal mass to be a benign teratoma and the tongue polyp, a hamartoma. The cleft palate was repaired at 15 and the trans-cranial dermoid cyst was resected at 27 months of age. Histologically, the dermoid cyst was lined by keratinised squamous epithelium and contained adnexal structures with no evidence of malignancy. At 3 years of age, the patient shows normal growth, development, neurological examination and baseline endocrine tests. She will need long-term neuroendocrine surveillance, specifically for precocious puberty and any recurrence of nasopharyngeal/intracranial pathology. This case report adds significantly to the growing body of literature on the clinical presentation and complex management of children with DPG-plus syndrome.

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P56

Case Report: Hypophysitis in a 9-year-old with Juvenile Idiopathic Arthritis - A Novel Association

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Introduction
Chronic autoimmune hypophysitis is a rare disorder characterised by prolonged inflammation of the pituitary gland, with the commonest subtype being lymphocytic hypophysitis. It is often associated with hypopituitarism and is exceedingly rare in the paediatric population. Here, the authors present a novel case of asymptomatic, chronic hypophysitis in a paediatric patient in association with juvenile idiopathic arthritis (JIA).
Case report
A 9 year-old Caucasian girl presented with a 4-month history of anterior uveitis, bilateral knee swelling and polyarthritis in the small joints. After a series of investigations, she was diagnosed with JIA (ANA positive, RF negative) and commenced on Adalimumab and Methotrexate treatment. An initial MRI orbit with contrast showed an enhancing mass centred within the pituitary fossa (10x11x13 mm), extending into the suprasellar cistern and superiorly displacing the pituitary stalk and optic chiasm. There was no associated hydrocephalus, bitemporal visual field defect or endocrine abnormality. Tumour markers (AFP, β-hCG) were negative. Genetic testing was negative for MEN1/AIP/CDKN1B/CDC73/ RET mutations. A biopsy was not performed due to potential damage to hypothalamo-pituitary function. Regular MRI scans over 2 years have shown no interval changes. Due to the diffuse pituitary enlargement and concomitant JIA, a provisional diagnosis of chronic autoimmune-related hypophysitis was made. This patient continues to undergo regular surveillance with yearly MRI scans.

Discussion
Lymphocytic hypophysitis in children can be either primary (often in association with other autoimmune disorders), or secondary (due to direct infiltration of the pituitary gland/stalk by tumours or other diseases e.g. Langerhans cell histiocytosis). Cases have been described in adults in association with rheumatoid arthritis, but none in children with JIA. Additionally, hypophysitis has been described in association with immune checkpoint inhibitors but not Adalimumab (anti-TNFα).
Conclusion
To the authors' knowledge, this is the first incidence of chronic autoimmune hypophysitis secondary to JIA in the paediatric population. Although this presentation was entirely asymptomatic, symptoms and signs of hypothalamic/-pituitary dysfunction in JIA patients should be investigated further and treated promptly.

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P57

Rapid-onset obesity, hypothalamic and autonomic dysregulation with neuroendocrine tumours: Can this be ROHHADNET?

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Introduction
ROHHADNET is a rare syndrome characterized by rapid onset obesity, hypoventilation, hypothalamic dysfunction, autonomic dysregulation and neuroendocrine tumours. Although obesity is the first recognisable feature, there is variable onset of other features, resulting in delayed or missed diagnosis, potentially leading to fatal consequences. We describe two cases with features of ROHHADNET, who had high heterogeneity in clinical spectrum.
Case-1
5-year old girl presented with rapid weight gain with BMI-SDS + 3 and suspected Cushing's syndrome. Her abdominal scan showed a paravertebral ganglioneuroma which was resected. She developed hypothalamic dysfunction at age 6 years with panhypopituitarism (thyroxine stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and growth hormone deficiency (GHD), with transient diabetes insipidus and subsequently, hypogonadotropic-hypogonadism. Autonomic dysregulation was evident as syncope, sweating and hypothermia. She had obstructive sleep apnoea (OSA) and prolonged QT syndrome. Her MRI pituitary and OGTT were normal. There was no response to immunoglobulin therapy. She remains under multidisciplinary team surveillance and was transitioned to adult service at 18-years.
Case-2
6-year old presented with obesity, BMI-SDS +2.8, was diagnosed with right suprarenal ganglioneuroblastoma, treated with surgery and chemotherapy abroad. She presented to our endocrine clinic in UK at 10 years of age with obesity (BMI-SDS +3.4), short stature, evolving endocrine dysfunction [hyperprolactinaemia (1800 U/l), GHD, TSH deficiency] and later developed hypogonadotropic hypogonadism with normal pituitary MRI. She had features of autonomic dysfunction (hypothermia and sweating). She was treated with cabergoline, growth hormone, thyroxine replacement and induction of puberty. At 15 years of age, she developed rapid weight gain (20 kg in 6 months; BMI 39.6 SDS 3.7), mild dyslipidaemia, and OSA. She awaits detailed respiratory assessment for BIPAP and immunomodulator therapy.
Discussion
ROHHADNET is mainly known to present with rapid onset obesity, as seen in both our cases. Although central hypoventilation is a recognized feature of this rare condition, we did not find conclusive evidence of hypoventilation in our cohort. However, the constellation of neuroendocrine tumour with central endocrinopathy and autonomic dysfunction were striking features suggesting ROHHADNET. Clinical features of ROHHADNET may vary and evolve over time. We propose a judicious MDT approach with early intervention to improve prognosis and life expectancy.

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P58

Management of cranial Diabetes Insipidus in a paediatric tertiary centre – clinical outcomes and patient perception of care

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There is growing recognition within Endocrinology physician and patient groups of morbidity and mortality in association with prescribing errors and dysnatraemia, in hospitalised patients with cranial diabetes insipidus (CDI). The study had two aims; firstly, to assess outcomes in hospitalised patients (paediatric and adult) with CDI by review of electronic records from 2012-2021, and secondly, to assess the same patient cohort's perceptions of their care via telephone questionnaire administered to patient or their parents. Eleven patients aged <18 years were included in the study (7 male), median age 13 (6-16) years. Median duration of CDI was 7 (1-12) years. Aetiology of CDI included hypothalamic-pituitary tumours (6), infiltrative disorders (2), and congenital (3). Route of desmopressin was oral in 9/11 patients. There were 21 admissions (33% emergency) to OUH in 7 patients, median length of stay 5 (1-16) days. Daily measurement of serum sodium was performed in 29% of admissions; hyponatraemia and hypernatraemia were noted in 33% and 29% of admissions respectively. Both hyponatraemia and hypernatraemia were noted in 19% of admissions. There were no cases of omission of desmopressin from the hospital drug-chart. Care was supervised by Endocrinology, or Endocrine consultation was sought in 84% of admissions post-2015. Five patients or their parents (45%) completed the questionnaire. Three patients (60%) self-reported one or more hospital admission since the diagnosis of CDI. One patient felt their medical team did not have a good understanding of the management of CDI during hospital admission, reporting confusion between CDI and diabetes mellitus in the hospital environment, leading to unnecessary blood glucose monitoring. No patient reported delay in administration of desmopressin in hospital although some reported frustration at a night-time dose of the drug being administered too early in the evening. Dysnatraemia is common in hospitalised paediatric patients with CDI. The majority of patients perceived that their medical team had a good understanding of CDI; this may be related to a high rate of Endocrine involvement compared with adult counterparts. A coordinated approach, including education of non-specialist hospital staff and early involvement by specialists, is needed to improve patient outcomes.

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P59

Lymphocytic Hypophysitis: A rare entity in children - Case report

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Introduction
Pituitary inflammation (Hypophysitis) is rare in paediatric population and usually results in pituitary enlargement and hypopituitarism. Hypophysitis can be either primary (most commonly lymphocytic, granulomatous or xanthomatous disease) or secondary (consequent to systemic diseases, immunotherapy or alternative sella-based pathologies). We describe the clinical presentation and management of apparent primary lymphocytic hypophysitis in an adolescent girl. Case report: A 16-year-old previously healthy girl presented with a 4 month history of headaches, vomiting and lethargy. Non-response to migraine treatment with beta blockers and sumatriptan culminated in MRI head, which identified a T2-hyperintense sellar/suprasellar lesion with a thick rim of enhancement and minimal sella expansion. Subsequent investigations showed hyperprolactinemia (1060mIU/l), TSH deficiency (fT4 7.4pmol/l, TSH 0.84mIU/l), and ACTH deficiency (30minute cortisol 287nmol/l on standard Synacthen test). Ophthalmological assessment showed normal visual acuity and fields. Treatment with hydrocortisone and levothyroxine was started. In view of proximity to the optic chiasm and uncertain diagnosis, our Pituitary Multidisciplinary Team agreed to proceed to trans-sphenoidal debulking and diagnostic biopsy. After opening the dura, yellowish necrotic pituitary tissue was observed and removed. Histologic examination showed non-neoplastic anterior pituitary tissue with prominent macrophagic and chronic lymphocytic inflammatory reaction. Although there were granulomata formation and cholesterol clefts suggesting inflammation secondary to ruptured Rathke's cleft cyst, there were no epithelial cells to support that diagnosis. Histology did not favour IgG4-related hypophysitis. Headaches

and lethargy completely resolved. Six weeks post-surgery, glucagon stimulation test was consistent with growth hormone (GH) deficiency and GH was started. At last review (3 months post-surgery), she was on multiple pituitary hormone replacements and was due post-operative surveillance MRI. Her menses had not yet restarted. Conclusion: Modern imaging techniques, histological classification and immune profiling have improved the accuracy of the diagnosis in patients with hypophysitis. Given the rarity of this condition in paediatric population, paediatric and young adult patients benefit from shared management with a multidisciplinary team involving adult Specialist colleagues. Careful follow-up is required to manage the endocrine deficiencies and seek to define a specific causal diagnosis if possible over time. A registry to understand the optimal management and outcomes of this rare condition is desirable.

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P60

Abnormalities of growth hormone secretion in lowe syndrome: a case series

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Background
Lowe Syndrome is an X-linked recessive genetic disorder caused by OCRL gene mutations, which impair intracellular trafficking processes. Signs are multi-systemic, including congenital cataracts, intellectual disability and proximal renal tubulopathy. Short stature is a common association, often attributed to chronic kidney disease through childhood. However, recent evidence suggests that the hypothalamo-pituitary-somatotroph axis may play a role.
Objectives
This case series reports three Lowe Syndrome patients with short stature and poor growth velocity at a tertiary-level centre in the United Kingdom (16yr, 18yr, and 5yr 11mo). All were diagnosed with GH deficiency or neurosecretory dysfunction through glucagon provocation tests, GH overnight profiling and/or pituitary MRI scans. All three were started on recombinant GH therapy at 15yr, 12yr 7mo and 4yr 2mo respectively (all pre-pubertal at commencement). This case series aims to analyse the efficacy of GH therapy in these patients.
Results
The first patient showed a reduced GH peak of 6.4ng/mL on provocation testing, and anterior pituitary hypoplasia on MRI. In response to GH therapy, his IGF-1 concentration doubled, puberty commenced, and growth velocity increased from 3.4 to 5.0 cm/yr. The second patient had a normal GH peak of 21.5ng/mL on provocation testing, but IGF-1 concentration was at the lower end of normal range at 106ng/ml (88-452ng/mL). He progressed well through puberty on GH therapy, with IGF-1 concentrations also doubling and growth velocity increasing from 2.8 to 4.9 cm/yr. The third patient had a normal GH peak of 11.2ng/mL on provocation tests, but undetectable IGF-1. The overnight profile was abnormal and anterior pituitary hypoplasia was identified. On GH therapy, growth velocity increased from 3.7 to 5.0 cm/yr and progression through shoes/clothes sizes hastened. However, IGF-1 levels remained low. Although these patients currently have heights $<$-3SDS, GH doses are still being optimized and delayed bone ages indicate further growth potential.
Conclusion
Short stature in Lowe Syndrome patients should not be presumed a consequence of renal failure alone. Aberrations of the hypothalamo-pituitary-somatotroph axis need to be considered. Recombinant GH therapy may improve linear growth, however, its impact on final height achieved is yet to be determined.

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Thyroid

P61

A rare variant of thyroid hormone receptor beta (THR β) gene mutation in a pre-school child

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Introduction
Resistance to thyroid hormone (RTH) is a rare inherited syndrome characterised by refractoriness of target tissue to thyroid hormone. Over 80% of cases are due to mutations in the thyroid hormone receptor beta (*THR β*) gene with over 100 mutations identified to date. The clinical manifestations vary from common feature as goitre to less common sinus tachycardia, learning disabilities, growth and developmental delay.
Aim
We report the case of a 4-year-old boy with incidental pick up of abnormally elevated free thyroxine and normal TSH biochemistry with absence of goitre or thyrotoxicosis features.
Case Presentation
4-year-old boy was referred to endocrine clinic following two-week history of lethargy, pallor, angular stomatitis. History suggested periods of hyperactivity, hand tremors, anxiety and poor weight gain with BMI 13.8 kg/m^2. There was no family history of thyroid disease, any safeguarding concerns or accidental ingestion. Investigations revealed normal full blood count, free thyroxine (fT4) of 86.6pmol/l (range 11-22) , fT3 of 23.9pmol/l (range 3.5 – 8.5) and TSH 2.59mu/l (0.7 – 6). Thyroid functions checked on alternate assay re-affirmed the same status. Heterophile antibody screen was negative. In contrast to the history, the child did not have clinical signs of hyperthyroidism or goitre. His heart rate, 24 hour ECG and Echocardiogram were normal. Chest x-ray showed normal cardiac and mediastinal contours. TSH Receptor Antibody (TRAb) was normal, making autoimmune thyroid disease less likely. A genetic panel screen for THR β gene mutation was considered which confirmed heterozygous THR beta mutation at Chr3:g.24164388A$>$G. This variant has been previously identified in only three additional patients with RTH. A genetic workup has been initiated for parents. He is asymptomatic without the need for any treatment at the 8-month follow-up.
Conclusion
Typically, children with THR β gene mutation have goitre and mild or no evidence of thyrotoxicosis. Our case demonstrates that one should consider RTH due to THR β when faced with biochemical findings of raised fT4, fT3 with normal TSH levels in the absence of clinical signs of thyrotoxicosis. Clinician's awareness can avoid unnecessary treatment which is not required in most cases, as the elevated thyroid hormones levels compensate for the partial tissue resistance.

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P62

Hypothyroid screening in children with down syndrome - a service evaluation

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Background
Individuals with Down Syndrome are at increased risk of developing thyroid disease. Given thyroid disorders represent a preventable cause of neurodevelopmental impairment, early detection and treatment are essential to maximise cognitive abilities in this already impaired population. This service evaluation sought to assess the efficacy of the Down Syndrome Hypothyroid Screening programme in its uptake and subsequent diagnosis of hypothyroidism.
Methods
A report of children with known Down Syndrome was obtained from the Greater Glasgow and Clyde Down Syndrome database. Children were excluded if they were $<$2 years or had been a resident for $<$2 years. Electronic Patient Records were used to access baseline characteristics and results of venous Thyroid Function Tests (TFTs). Data on TSH capillary screening were obtained via the Scottish Newborn Bloodspot Screening lab. Data were collected on each child's previous 3 screening and the time between screening was calculated. From this, children referred to Endocrinology following abnormal screening and those subsequently commenced on Levothyroxine therapy were identified.
Results
We identified 248 children with Down Syndrome (122 male). 20 children were excluded as they were $<$2 years old or residents for $<$1 year. This left 228 children (114 male). The mean age was 9.9 years, range (2.1-22.7). 3 children received no screening in their lifetime. Of those screened, 92% received screening within the last 1.0 decimal years (207/225) and a further 3.1% (7/225) received screening within the last 1.5 years. 7 of the 225 children had been screened once (n=218). 74 children (33.9%) had 1.0 years or less between their previous screenings. A further 118 children (54.1%) had 1.5 years or less between each

screen. 21 children (9.3%) had abnormal screening, with 20 children referred to Endocrinology. One child had normal TFTs and was not referred. Of the 21 children with abnormal screening, 16 (76.2%) were commenced on Levothyroxine therapy.
Conclusion
Within Greater Glasgow & Clyde, the hypothyroid screening programme is effective in monitoring and detecting thyroid disease. The majority of children with Down Syndrome receive hypothyroid screening annually. Of those screened, 9.3% had abnormal screening results, with 76.2% of these children commenced on Levothyroxine therapy.

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P63

Conversion of hypothyroidism to hyperthyroidism – an interesting U-turn

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Background
Hashimoto's thyroiditis and Grave's disease are the common autoimmune diseases of thyroid gland across all age groups. Some patients with autoimmune hyperthyroidism can become hypothyroid however it is rare for patients with hypothyroidism to develop Grave's disease. Although some cases have been reported in adults, this phenomenon is very rare in the paediatric age group.
Case
13 year old Caucasian girl who was diagnosed with aplastic anaemia and treated with bone marrow transplant two years ago was referred to our endocrine clinic with history of neck swelling. On examination she had grade 2 goitre. Her initial investigations showed low Free T4 6.5pmol/l (9.0- 25.0), raised TSH $>$150 mIU/l (0.3-5.0) with elevated thyroid peroxidase (TPO) antibodies 329 IU/ml (0 -60). She was diagnosed with hypothyroidism secondary to Hashimoto's thyroiditis and commenced on levothyroxine. The dose of levothyroxine was titrated to 100 mg once daily and her condition was stable for eighteen months. On routine monitoring, her Free T4 was raised (34 pmol/l) and TSH suppressed ($<$0.05 miu/l). She remained asymptomatic with no signs of hyperthyroidism. After excluding possibilities of drug overdose and drug interactions, the repeat thyroid function test (TFT) showed similar findings. The dose of Levothyroxine was weaned over next few months and eventually stopped. After 4 weeks her repeat TFT was still suggestive of hyperthyroidism {Free T4 43 pmol/l, TSH $<$0.05 miu/l and Free T3 22.6 pmol/l (3.5-6.5)}. She also developed increased sweating, palpitation, tiredness and sleep disturbance. We commenced her on Carbimazole and propanalol. Her Anti TSH receptor antibodies was positive 4.4 IU/l (0- 0.09) confirming a diagnosis of Grave's disease. Her symptoms improved and she was maintained euthyroid on carbimazole 20 mg once daily. Her USS thyroid did not show any thyroid nodules.
Discussion
The pathophysiology for this rare transition is not clear and few hypotheses have been postulated in the literature. One of them was switching of balance between the types of TSH receptor antibodies from blocking to stimulating antibodies (1).
Conclusion
Patients with established autoimmune hypothyroidism can rarely develop hyperthyroidism. Hence regular monitoring of TFT and improved awareness about this phenomenon is important.

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P64

Relapse of childhood Graves' disease despite normalization of TSH Receptor Antibodies

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Introduction
The long term remission rate of Grave's disease in children after anti-thyroid drug (ATD) therapy is around 30% as opposed to 40-60% in adults. There still exists a controversy regarding the duration of medical treatment and the markers of long term medical remission that support cessation of therapy. Normalization of TSH Receptor Antibody (TRAb) level is considered to be a favourable marker for remission prior to stopping therapy. We report two patients who received prolonged ATD therapy, remained euthyroid during therapy and had normalization of TRAb levels despite which they relapsed after stopping therapy.
Case 1
A nine year old girl presented with palpitations, weight loss and a goitre alongwith mild exophthalmos and eye pain. Investigations revealed raised FT4 and suppressed TSH. She received Propranolol and a 'block and replace' regimen with Carbimazole and Levothyroxine for 4 years. She responded well and remained euthyroid during therapy. Treatment was stopped after documenting negative TRAb levels ($<$0.3 IU/l) which were previously raised (1.6 IU/l, normal range $<$0.9 IU/l). She relapsed after a year of treatment cessation with raised TRAb (2.6 IU/l).
Case 2
A seven year old girl presented with increased appetite without weight gain, rapid growth, exophthalmos and goitre, with tachycardia noted on examination. Her blood results confirmed hyperthyroidism. She was treated with Propranolol, and then with Carbimazole and Levothyroxine for 3 years with good response but relapsed 4 months after they were stopped. She was restarted on ATD therapy for another 4 years. Her initial TRAb levels were very high (49.5 IU/l) but were negative ($<$0.3 IU/l) prior to stopping treatment the second time. However, she relapsed again after 6 months with raised TRAb (5.6 IU/l).
Conclusion
We describe 2 patients who relapsed after prolonged ATD therapy despite normalization of TRAb level prior to cessation of treatment. TRAb levels can go from negative to positive during a relapse and so should continue to be monitored after cessation of treatment. More work is required to establish reliable indicators of long-term remission in childhood Graves' disease.

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Audit of the identification and management of congenital hypothyroidism in a single centre

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Introduction
Congenital hypothyroidism (CHT) is a significant health issue, responsible for serious long-term consequences if left untreated. From experience we know that early identification and treatment can prevent long-term neurodevelopmental sequelae of the condition. We audited our management of babies born with CHT between the years of 2012 and 2019 to evaluate our care against best practice.
Methods
Babies born with CHT in Nottingham between 2012–2019 were identified using a local patient database and the newborn screening laboratory database. Electronic records were reviewed, gathering data on demographics and clinical management to assess adherence to the UK newborn screening programme clinical referral standards and guidelines.
Results
Twenty-eight babies were identified and a complete data set was obtained for 22 patients. The mean age at identification was 20 days. The majority of referrals came through the newborn screening laboratory (79%) with the remainder from neonates (18%) and A&E (4%). 82% of babies were reviewed within 24 h. All had repeat blood samples to confirm the diagnosis. 61% were started on a dose of 10-15 micrograms/kg/day. Normalisation of the TSH was achieved within four weeks in 62% of babies, but only 9% had normalisation of their fT_4 by two weeks. Treatment was started by 14 days of age in only 40% of those suspected with CHT. 71% were transient and 29% had permanent CHT following a trial off medication. 18% had imaging, of which 60% were normal, 20% were abnormal and 20% inconclusive.
Conclusion
The data indicates that time to review from identification was performed well, although less than 50% of babies were started on treatment within the two-week timeframe. This may be due to delayed identification, with a mean age at identification of 20 days. Although most received a dose of 10 micrograms/kg/-day, several were underdosed, leading to a delay in the normalisation of thyroid function. The majority of patients had normal ultrasound scans. Delays in identification suggest a review of the pathway of care would be useful, and variations in dosing and imaging could be streamlined with the formulation of a guideline.

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