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37th Meeting of the British Society for Paediatric Endocrinology and Diabetes 2009

Speaker Abstracts

S1

What the new UK-WHO growth charts mean to you

Charlotte Wright
University of Glasgow, Glasgow, UK.

New UK growth charts using the new WHO standard for children from birth to four years should now be used for all babies born in England after May 11th 2009 (October 2009 in Scotland).
The WHO charts for the first time describe optimal rather than average growth, set breast feeding as the norm and are suitable for all ethnic groups. UK children fit the new charts well for length and height but will look appear relatively heavier by the age of one. This will mean that only around 0.5% children be below the weight 2nd centile and that weight centile falls will be much less common.
The new charts are going to look different and chart users need to familiarise themselves with the changes: there will be a disjunction at age 2 years when the WHO standard changes from length to height; parents tend to expect all healthy children to be on the 50th centile so this is no longer emphasised, but there are more subtle indicators of the 50th percentile.
The charts now include detailed instructions which draw on research evidence and UK policy on screening and referral. They define when a measurement or growth pattern is outside range of normality and advise when further assessment is advisable.
A new low birth weight chart is also available for very preterm and small infants. This uses a novel, simpler method of gestational correction and will be useful for all sick or vulnerable infants, as it is low reading and large scale.
The charts, educational materials and fact sheets are all freely downloadable from www.growthcharts.rcpch.ac.uk.

S2

New UK preterm growth charts

Tony Williams
London, UK.

Abstract unavailable.

S3

Current approaches to understanding the pubertal growth spurt

Tim Cole
UCL Institute of Child Health, London, UK.

The pubertal growth spurt involves a rapid increase then decrease in height velocity (HV), where both the timing and intensity of the spurt vary considerably between individuals. The analysis of such growth curve data is an ongoing statistical problem. Current approaches involve fitting say the Preece–Baines (PB) curve to each individual's data, and summarising the curves by averaging the five fitted PB parameters across individuals. But this has two drawbacks: fitting lots of separate curves, and needing as many as five parameters per individual.
The talk will present an alternative model of pubertal height growth, due to Beath and called SITAR, where just ***one*** growth curve is fitted that applies to all individuals. Growth curves for Individuals are matched to the average curve by shifting their curve up-down (representing differences in pre-pubertal size) and left-right (for differences in tempo or age at peak HV), and the age scale is also stretched or squashed (indicating how fast time passes in the individual, i.e. velocity). These three parameters per individual are estimated as random effects at the same time as fitting the average curve, and the goodness of fit of the model matches that of individually-fitted PB curves. The outcome is a cubic spline growth curve that applies to all subjects, plus triplets of parameters per individual (size, tempo and velocity) that summarise their departures from the mean curve.
Two datasets were used to demonstrate the method: $N=3245$ boys from Christ's Hospital (CH) School recruited 1939–68 and measured twice a term from 9 to 19 years ($n=129\,508$), and $N=92$ Turner syndrome (TS) girls from the UK Turner Study measured 6-monthly from 9 to 16 years ($n=1102$).
The growth curve model explained 99% of the variance in both datasets (RSD 6–7 mm). In CH, growth tempo (but not size or velocity) was strongly associated with IGF1 measured 50 years later ($P=0.0004$, $N=1014$). The TS girls randomised to receive oxandrolone from 9 years did not differ from the placebo group in terms of size or tempo, but their velocity was highly significantly increased ($P<10^{-8}$).
The SITAR growth curve model is a major step forward in the analysis of pubertal growth.

S4

Investigating peripubertal growth problems

Mehul Dattani
UCL Institute of Child Health, London, UK.

The investigation of growth failure can be fraught with difficulties at all ages, but never more so than in the peri-pubertal period. The differential diagnosis at this period of life includes constitutional delay of growth and puberty (CDGP), hypogonadotrophic hypogonadism (HH), GH insufficiency (GHD/GHI) and a physiological peri-pubertal reduction in growth velocity in addition to other organic causes of growth failure. Careful auxology and pubertal staging with assessment of growth velocity over a period of at least 6–12 months is usually required before making a decision to investigate a child. A decision is made to investigate a child if the height is more than 2 S.D.s below the mean, or if the child is more than 1.4 S.D.s below the mid-parental height, in conjunction with a poor growth velocity. The NICE guidelines recommend the performance of at least two tests of GH secretion, once other causes of growth failure have been excluded. Physiological tests lack reproducibility and are poorly validated; hence provocative testing remains the most widely used and accepted method of diagnosing GHD. A large number of provocative tests are available for use, and there is little or no consensus as to the most reliable tests. Lack of reproducibility, lack of normative data leading to the use of arbitrary 'cut-off' values, GH assay variability, and possible hazardous complications add to the controversy surrounding the tests and their interpretation. Obesity is associated with a reduction in GH secretion, often resulting in false positive results. Additionally, there is no consensus with respect to the use of sex steroid priming. The use of the GH-dependent growth factors IGF1 and IGFBP3 in isolation lacks sensitivity and specificity, but in combination with provocative tests of GH secretion, can be associated with acceptable sensitivity and specificity. More recently, the use of MRI to visualise the hypothalamo-pituitary axis has helped as an adjunct to the diagnosis of GHD; the presence of an ectopic posterior pituitary is highly predictive of GHD. The use of the GnRH test in combination with HCG stimulation may help in confirming a diagnosis of HH in isolation or combined with GHD. Finally, recent advances in molecular genetics may help in clarifying the diagnosis, with the identification of a number of genes implicated in the aetiology of GHD or HH. To conclude, the assessment of growth failure in the peri-pubertal period is associated with considerable diagnostic uncertainty, and likely requires a combination of GH provocation, measurement of IGF1 and IGFBP3 concentrations, neuroimaging and molecular genetics in order to achieve an acceptable sensitivity and specificity.

S5

Achieving the best growth at puberty in Turner syndrome

Malcolm Donaldson
Glasgow, UK.

Abstract unavailable.

S6

Insulin therapy at school

Julie Edge
John Radcliffe Hospital, Oxford, UK.

Diabetes control is poor in children in the UK with fewer than 20% of children achieving target HbAlc levels. Multiple injection therapy and insulin pumps produce the most physiological blood glucose control but both require the child to have blood glucose testing and insulin dosing at each meal and most snacks, and therefore at school. There are often huge obstacles to setting appropriate support in place in schools, particularly in children who are too young to perform their own injections and blood glucose testing, even under supervision. Many studies have now shown that glycaemic control is related to complications, even in young children, and that intensive insulin regimens result in improved control and reduced complication rates. We cannot therefore allow the fact that schools are reluctant to take on diabetes care, to be a reason for delaying the introduction of such regimens. Fortunately individual parents have started to lobby for change because of the problems they have encountered in school.
Schools now have increasing obligations under various legislation to ensure that they do not discriminate against pupils or put them at a disadvantage because of their health. It is perhaps not widely appreciated how much of an adverse impact on education badly-controlled diabetes can have, and so this is indeed an educational issue. However there is no obligation on teachers to help with

administering medicines – this must be done by volunteers. Schools can employ a support worker with the role of administering insulin injections in the job description but this requires funding.
The main obstacles to schools taking this on appear to be a lack of knowledge and understanding of the importance of diabetic control, and fear of adverse incidents and litigation, all of which can be overcome by explanation and education. Indeed, once the volunteers in schools understand the reasons for the injections and blood tests, and they have been adequately taught in the practical skills, schools are generally keen to help the individual child. Indemnity cover for all school staff can be provided by the Local Authority, which will insure all staff for their activities in administering medications. Education is the key, and we should all start now.

S7

Cystic fibrosis related diabetes (CFRD) in childhood and adolescents

Stephen O'Riordan
The Institute of Child Health, UCL, London, UK.

Life expectancy has improved for all children and adolescents with cystic fibrosis (CACF); children now survive into adult life. Cystic fibrosis related diabetes (CFRD) is increasing[1–3]. The combination of CF and diabetes has a negative impact on survival. From 2002 to date, CFRD has been related to decreased survival[3] and survival gender differences are also described[4]. Patients with CFRD have a sixfold increase in morbidity and mortality[3].
CFRD is usually asymptomatic and can remain undetected for up to 4 years prior to diagnosis. Recent International Society of Pediatric Diabetes Consensus Guidelines on CFRD highlight the use of continuous glucose monitoring (CGM) in the normal glucose tolerance (NGT) and impaired glucose tolerance (IGT) stages may be important in early diagnosis of CFRD[5]. CGM has also been validated for use in children and adolescents with CF[6]. Early insulin therapy in CF improves growth, lung function and reduces the number of chest infections[7]. Diabetes is now the most common morbidity in CF patients, some reports estimate 50–75% will be diagnosed with CFRD by the age of 30 years. Early detection and identification of abnormalities in glyceamia in CF is essential by all screening methods.
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S8

Sport for teenagers with diabetes

Francesca Annan
Liverpool, UK.

Abstract unavailable.

S9

Child protection issues in children and young people with diabetes

Sarah Steele
Southampton, UK.

Abstract unavailable.

Oral Communications

Oral Communications 1

OC1.1

Cholesterol and apolipoprotein levels in a cohort of girls with Turner syndrome, and the effect of GH therapy

Chris Gardner, Anne Garden, Mohammed Didi, Paul Newland, Indi Banerjee & Jo Blair
Alder Hey Children's NHS Foundation Trust, Liverpool, UK.

Introduction
Ischaemic heart disease occurs seven times more frequently in women with Turner syndrome (TS) than the normal population. Adult TS subjects have raised serum cholesterol (Ch). In our service we measure Ch, apolipoprotein A1 (APA) and B (APB) annually in TS patients aged >5 years as APB:APA in childhood is a strong predictor of cardiovascular risk in adult life. Little is known about lipid profiles or the effects of GH or oestrogen (E_2) in childhood TS.
Methods
Retrospective study of serum Ch, APA, APB and APB:APA collected at annual review.
Objectives
1) To describe serum Ch, APA and APB SDS in childhood; 2) to examine associations with GH and E_2 treatment.
Results
Of 68 results from 34 subjects age (mean ± 1S.D.) 13.3 ± 3.87 years at sampling were analysed. Serum Ch SDS was significantly higher in subjects aged >12 years than younger subjects (1.39 ± 0.63 vs 0.35 ± 1.16, $P=0.02$), persisting after correction for body mass index. There was no significant difference in APA, APB or APB:APA SDS. In regression analysis (GH versus no GH), GH was associated with an increase in APA SDS (0.04 ± 0.90 vs −0.85 ± 0.69 $R^2=0.159$, $P=0.03$) and reduction in APB:APA SDS (0.13 ± 0.71 vs 1.12 ± 1.82 $R^2=0.178$, $P=0.016$) but not Ch or APB SDS (Ch 0.86 ± 1.46 vs 0.85 ± 1.39 $R^2=0.07$, $P=0.34$, APB 0.17 ± 0.86 vs 0.32 ± 1.1 $R^2=0.055$, $P=0.475$) when controlling for age, BMI SDS and treatment with E_2. In subgroup analysis, the association of GH with APA and APB:APA remained significant. E_2 treatment was not associated with significant changes in lipid profiles.
Conclusion
The increase in serum Ch in adult TS subjects appears to have its origin in childhood. Treatment with GH is associated with a more favourable APB:APA and may have a role in improving cardiovascular risk in these subjects.

OC1.2

Altered GH/IGF1 signalling in children born small for gestational age without catch up growth

Imogen Butcher[1], Andrew Whatmore[1], Philip Murray[1], Melissa Westwood[2] & Peter Clayton[1]
[1]Endocrine Science Research Group, University of Manchester, Manchester, UK; [2]Maternal and Fetal Health Research Group, University of Manchester, Manchester, UK.

Background
Infants born small for gestational age (SGA) usually show catch-up growth during the first few years of post-natal life. However, some infants remain small and little is known about the factors governing their growth failure. GH and IGF1 receptor mutations only account for a minority of cases. We have now initiated an *in vitro* assessment of signalling molecules downstream of these receptors and evaluation of cell growth characteristics.
Method
Skin biopsies were obtained with local ethics approval from healthy children ($n=3$) and SGA children without post-natal catch up growth ($n=3$). Fibroblasts were isolated and serum starved at sub-confluence for 24 h. Cells were then stimulated with IGF1 (100 ng/ml) or GH (200 ng/ml) for 0, 15 and 30 min. The expression and activation of the signalling molecules Stat5b, Akt and MAPK were assessed by western blotting using antibodies that recognise either the total or activated isoforms of these proteins. Cell growth was defined by cell counting and Brdu incorporation, and apoptosis by TUNEL staining.
Results
Stat5b, Akt and MAPK were present in cells from both control and SGA children. Stat5b activation was decreased in SGA cells when compared to controls however activation of MAPK appeared to be similar in these two cell types. A different pattern of IGF1 stimulated Akt phosphorylation was found and we have demonstrated that activation of Akt 2 occurs in SGA cells and not in control cells. Cell growth was not different between normal and SGA cell lines. However, apoptosis was significantly increased in SGA cells.
Conclusion
GH and IGF1 signalling pathways and rates of apoptosis appear to be altered in SGA children without post-natal catch up growth. This may be indicative of a causative factor for post-natal growth retardation, or a cellular response/compensatory mechanism to the retarded growth seen in these children.

OC1.3

IGF1R gene expression in patients with idiopathic short stature according to GH and IGF1 status

Soraya Sader Milani, Rodrigo Custódio & Carlos Eduardo Martinelli Jr
Department of Paediatrics, School of Medicine of Ribeirão Preto, University of São Paulo, Ribeirão Preto/São Paulo, Brazil.

The aim of this study was to analyze IGF1R gene expression in patients with idiopathic short stature (ISS) and correlate it with their GH and IGF1 status. In a previous study, we reported lower final height in subjects with ISS and GH peak ≥40 mU/l (Group1, $n=16$) compared to those with ISS and GH peak between 20 and 40 mU/l (Group2, $n=15$), after stimulation test (ITT) performed before or during puberty. Patients were 16–24 (Group1) and 15–26 (Group2) years old when recalled for measurements of final height, BMI, serum IGF1 and biochemical determination. At these time whole blood sample were obtained for IGF1R gene expression analysis. While most of Group2 patients had serum IGF1 concentrations around the mean (±1S.D.) Group1 patients had IGF1 mainly above +1S.D. (Group1a) or below −1S.D. (Group1b) ($P<0.05$). These 3 groups of patients (1a, 1b and 2) showed different BMI and lipid profile suggesting different status of GH–IGF axis activation: partial IGF insensitivity, partial GH insensitivity and normal GH–IGF axis, respectively. The possibility of different expression of IGF1R among these subjects was then considered. The levels of mRNA expression of the IGF1R gene in peripheral leucocytes were analyzed by quantitative real-time PCR and a cut-off for $2^{-\Delta\Delta C_T}=2.0$ was assumed. IGF1R gene expression was higher in Group1 than in Group2 patients ($P=0.03$). However, no difference in IGF1R mRNA expression comparing Group1a to Group1b was observed. In conclusion, patients with ISS and high GH peak during stimulation test expressed more IGF1R mRNA than those with GH peak between 20 and 40 mU/l. It could reflect an up-regulation mechanism in attempt to compensate reduced IGF1 action due to either low IGF1 levels or poor signaling. These findings reinforce the existence of different subgroups of patients under the label of ISS that must be better characterized to allow a better clinical approach.

OC1.4

A multisystem disorder associated with defective selenoprotein synthesis and a thyroid signature

R Padidela[1], N Al-Ali[2], E Schoenmakers[2], M Agostini[2], O Rajanayagam[2], M T Dattani[1] & V K K Chatterjee[2]
[1]Developmental Endocrinology Research Group, Institute of Child Health and Great Ormond Street Hospital for Children, London, UK; [2]Institute of Metabolic Science, University of Cambridge, Cambridge, UK.

The superfamily of ~25 human selenoproteins includes antioxidant and oxidoreductase enzymes together with other proteins of unknown function. We describe a child with a multisystem disorder involving deficiencies of several selenoproteins, identified on the basis of abnormal thyroid function.
A 3.6-year-old male was referred with elevated free thyroxine (FT_4 – 44.4 pmol/l (*N* 12–22)), low free triiodothyronine (FT_3 – 1.9 pmol/l (*N* 5.2–10.2)) and normal TSH (2.9 mU/l (*N*<6)) concentrations, indicating reduced T_4 to T_3 conversion. Deiodinases (DIOs) are selenoenzymes, and low circulating selenium 0.06 μmol/l (*N* 0.5–1.3), undetectable glutathione peroxidase (GPx) and reduced selenoprotein P concentrations, suggested multiple selenoprotein defects. Incorporation of selenocysteine (Sec) during protein synthesis requires binding of a multiprotein complex that includes the selenocysteine insertion sequence binding protein 2 (*SECISBP2*) to a stem loop structure in the 3′-untranslated region of their mRNAs. *SECISBP2* gene sequencing identified a heterozygous missense mutation (Cys691Arg) in the proband and his mother, involving a highly conserved cysteine residue within the C-terminal RNA-binding domain of this protein; an additional defect, involving aberrant *SECISBP2* splicing, was identified in the proband's other allele and his father.
Additional features in the index case included short stature (height −2.4SDS), mild global developmental delay, and proximal muscle weakness. Selenoprotein N (SEPN) is essential for normal muscle function, and SEPN expression was markedly reduced in cultured fibroblasts from the proband. Progressive failure to thrive in infancy led to a diagnosis of eosinophilic colitis at 24 months. Body composition was abnormal, with markedly increased fat mass (+2SDS), but associated with a propensity to non-ketotic fasting hypoglycaemia requiring supplementary enteral nutrition. Auditory assessment suggested bilateral high

frequency hearing loss, which is also a feature in DIO2 null mice. Normalisation of FT_3 levels following commencement of liothyronine treatment, was associated with improvement in linear growth, speech and neurodevelopment.
This unusual genetic disorder highlights the diverse roles of selenoproteins in biological processes and may also be a useful paradigm to model consequences of human selenium deficiency.

OC1.5

The primordial growth disorder 3-M syndrome connects ubiquitination to the cytoskeletal adaptor obscurin-like 1

D Hanson[1], P G Murray[1], A Sud[1], S A Temtamy[2], M Aglan[2], A Superti-Furga[3], S E Holder[4], J Urquhart[1], E Hilton[1], F D C Manson[1], P Scambler[5], G C M Black[1] & P E Clayton[1]
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3-M syndrome is an autosomal recessive primordial growth disorder characterized by pre- and post-natal growth restriction, facial dysmorphism and radiological abnormalities. Mutations in the gene *CUL7* have been previously shown to cause 3-M syndrome. CUL7 is a member of the cullin family of E3 ubiquitin ligases involved in targeted protein degradation.
We identified a large cohort of 3-M syndrome patients who did not carry *CUL7* mutations but shared the same distinctive phenotypic features. Genome wide high density SNP mapping identified a second locus on chromosome 2q35–q36.1. Subsequent candidate gene analysis led to the identification of 7 distinct null mutations from 10 families within the gene encoding Obscurin like-1 (*OBSL1*). OBSL1 is a putative cytoskeletal adaptor protein which we have shown localizes to the nuclear envelope and is homologous to the giant sarcomere protein Obscurin.
We have been able to demonstrate that OBSL1 interacts with CUL7 by co-immunoprecipitation of transiently expressed HEK293 cells. In addition knockdown of *OBSL1* by siRNA in these cells leads to the concomitant loss of CUL7. Morpholino (antisense oligonucleotide) induced knockdown of the Obsl1 ortholog in *Xenopus tropicalis* causes significant growth restriction but otherwise phenotypically normal tadpoles at embryonic stage 50 (14 days).
To our knowledge we report the first identification of mutations in *OBSL1* and first involvement of a cytoskeletal adaptor protein in a human growth disorder. Our findings imply that CUL7 and OBSL1 are involved in the same molecular pathway and this pathway is a key regulator of human growth. A small cohort of 3-M syndrome patients with neither *CUL7* nor *OBSL1* mutations has also been identified suggesting a third gene is likely to be involved in the CUL7/OBSL1 pathway.

OC1.6

Influence of JAK2 and PI3 kinase genotypes on growth response to GH therapy

A Omokanye, M Solomon, R Morjaria, P Murray, A Whatmore, L Patel & P Clayton
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Carriage of the exon 3 deletion in the GH receptor (GHR) gene has been reported to enhance growth response to GH therapy. JAK2 and PI3K are involved in signal transduction from the GH (JAK2/PI3K) and IGF1 (PI3K) receptors. We have investigated whether a single nucleotide polymorphism within these genes influences growth response to GH therapy. DNA was taken, with ethical approval, from 104 children treated with GH therapy. Diagnoses were: GHD ($n=44$), TS ($n=23$), SGA ($n=15$), PWS ($n=9$), ISS ($n=4$), SD ($n=4$) and CRI ($n=5$). Clinical and auxological data were obtained from case records. We examined the 97348G/A polymorphism in exon 19 of JAK2 and the 73167G/A polymorphism in exon 15 of PI3Kinase catalytic subunit α (PI3KCA), by PCR and subsequent restriction enzyme digestion. Factors influencing change in height SDS over 2 years were assessed by backwards linear regression (independent variables: genotype, mean parental height SDS, birth weight SDS, age at start of GH treatment, starting height SDS, starting BMI SDS, starting GH dose, and mean GH dose over 2 years). Genotype frequencies for JAK2 were AA=23, AG=76 and GG=5. Genotype frequencies for PI3KCA were AA=0, AG=54 and GG=50. JAK2 and PI3K genotype did not feature in prediction models during analysis of all patient data, irrespective of diagnosis. However, PI3K genotype did feature in the prediction model for the GHD cohort. In the absence of genotype this prediction model accounted for 36% of the variability in growth response. By including genotype an improved model, accounting for 51% of the variability, was derived. The PI3KCA 73167G/A polymorphism appears to influence growth response to GH, in GHD patients. A systematic approach to assess the effect of multiple genes related to GH/IGF1 signalling pathways should be undertaken to evaluate their genetic contribution to growth response for patients receiving GH therapy.

Oral Communications 2

OC2.1

Final height in Turner syndrome after Oxandrolone and delayed pubertal induction: results of a UK randomised, double-blind, placebo-controlled trial

Emma-Jane Gault[1], Rebecca Perry[2], Sarah Casey[2], Tim Cole[3], Wendy Paterson[2], Peter Hindmarsh[3], Peter Betts[4], David Dunger[5] & Malcolm Donaldson[1]
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The UK Turner Study examined in girls with Turner syndrome (TS) the impact on final height (FH) of Oxandrolone (Ox) and/or delayed pubertal induction (14y).
Methods
Girls with TS aged 7–13y receiving GH were randomised to Ox (0.05 mg/kg per day, max. dose 2.5 mg/day) or placebo from 9y (or from enrolment if >9y). Girls requiring oestrogen were further randomised to begin oral Ethinylestradiol (E_2) (Y1:2 μg/day; Y2:4 μg/day; Y3:4 months each of 6/8/10 μg/day) at 12y or 14y. Analysis was by multiple regression.
Results
From 1999 to 2003, 106 girls were recruited at 36 UK hospitals. Fourteen withdrew, and 75 have reached FH. The table gives characteristics of girls by randomisation and outcome.

Table 1

	1st randomisation		2nd randomisation	
Mean (s.d.)	Ox	Placebo	E_2 at 12y	E_2 at 14y
At enrolment	***(n=51)***	***(n=55)***	***(n=29)***	***(n=31)***
Age (y)	10.3 (1.6)	10.3 (1.6)	9.6 (1)	9.7 (1.2)
Height (cm)	126.7 (8.5)	125.6 (7.9)	122.8 (6.9)	124.2 (6.7)
Age at GH start (y)	7.0 (2.5)	6.9 (3.0)	6.7 (2.1)	5.5 (2.3)
At final height	***(n=35)***	***(n=40)***	***(n=22)***	***(n=20)***
Age (yrs)	16.4 (1.3)	16.6 (1.3)	16.3 (1.1)	16.8 (0.9)
FH (cm)	154.0 (4.8)	148.9 (6.2)	149.3 (7.0)	153.2 (4.4)

Ox and 14y-induced puberty both increased FH, by 5.0 cm ($P=0.0002$, $n=75$) and 3.7 cm ($P=0.03$, $n=42$) respectively. The interaction between them was negative and close to significance ($P=0.06$, $n=42$) with these FH effects: Ox vs no Ox (E_2 at 12y), 8.2 cm; E_2 at 14 vs 12y (no Ox), 6.4 cm; Ox/E_2 at 14y vs no Ox/E_2 at 12y, 8.4 cm. No significant adverse events such as voice deepening or clitoromegaly were reported.
Conclusions
Ox and pubertal induction at 14y both have a positive effect on FH in TS but the effects are not additive so there is little advantage in using both. Ox is a realistic alternative to late pubertal induction for increasing FH.

OC2.2

Recombinant human GH improves linear growth in children with inflammatory bowel disease: results of a randomised controlled trial

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Background
Despite optimal management, children with inflammatory bowel disease (IBD) may suffer from growth retardation. The role of rhGH in these children is unclear.

Design
Randomised controlled trial of rhGH (0.067 mg/kg per day) for 6 months.
Subjects
Twenty-two children with IBD and HtSDS < -2 or HtSDS < -1 and HVSDS < -1. Eleven were in the control group (C) and eleven in the treatment group (Rx).
Methods
HtSDS, HV, HVSDS were compared between in Rx and C at baseline (T0) and 6 months (T6). HVSDS was adjusted for Tanner stage (TS) for girls ≥ 11 years and boys ≥ 12 years. Glucose homeostasis was assessed by fasting glucose, insulin and HbAlc. All data are expressed as median (10th, 90th).
Results
CA at T0 was 14.7 years (9.3, 16.2) and 13.7 (9.1, 15.5); median CA-BA at T0 was 1.7 years (-0.3, 3.6) and 1.7 years (-0.7, 4.1) for Rx and C. Pubertal progress was noted in 5/11 and 3/11 of Rx and C. HtSDS at T0 was in Rx and C: -2.8 (-4.1, -1.5) and -1.8 (-2.7, -1.3), ($P=0.001$). Change in HtSDS at T6 in Rx and C was significantly different: 0.3 (0.1, 0.8) and -0.1 (-0.3, 0.3), $P<0.0001$. HV at T0 was similar in Rx and C: 5.0 cm/year (0.8, 8.8) and 3.8 cm/year (1.6, 6.5) and so was HVSDS: -3.1 (-6.0, 4.4) and -2.4 (-6.2, 1.8). HV at T6 in Rx and C was 10.8 cm/year (6.1, 14.3) and 3.5 cm/year (2.0, 9.3), $P<0.0001$. HVSDS at T6 in Rx and C was 3.2 (-0.4, 16.4) and -2.0 (-6.3, 4.9), $P=0.0001$. CRP, ESR, Alb, Hb and cumulative prednisolone dose were similar between the Rx and C at T0 and T6. ΔBA/ΔCA was similar in the two groups at T6. At T6, in Rx and C, fasting insulin, was 7.0 mU/l (2.1, 15.7) and 3.8 mU/l (2.1, 6.6), $P=0.04$ and HOMA index was 1.5 (0.3, 3.7) and 0.3 (0.2, 0.8), $P=0.05$. Fasting glucose and HbAlc, were similar in both groups at T6.
Conclusion
rhGH in children with IBD and growth retardation can increase HV by over 100% without excessive skeletal maturation. It may be associated with a reduction in insulin sensitivity but there is no overt abnormality of glucose tolerance.

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OC3.1

Accuracy of 2.5 mg hydrocortisone doses from quatered 10 mg tablets

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Introduction
In paediatric practice hydrocortisone (HC) is frequently prescribed in doses of ≤ 2.5 mg. HC tablets are only available in 10 mg strengths or as 2.5 mg Corlan pellets, a formulation designed for oro-mucosal delivery. Thus, tablets are segmented to obtain an appropriate dose. This study examines the accuracy of obtaining 2.5 mg HC doses from quartered tablets.
Materials and methods
Of 10 mg Hydrocortone tablets were studied. Weight uniformity of whole and quartered tablets was assessed. Tablets were quartered using a tablet cutter to mimic the manipulations undertaken prior to drug administration. HC content of each quarter was determined by HPLC.
Results
The mean intact tablet weight was 245.9 ± 2.5 mg ($n=10$) with a coefficient of variation (CV) of 1.0%. The mean quartered weight was 56.7 ± 7.6 mg ($n=144$ quarters), CV 13.4%. The ranges of these values were 38–68 mg. The anticipated quarter weight was 61.5 mg indicating an average loss of 4.8 mg. The mean HC content for the 144 quarters was 1.85 ± 0.55 mg, CV 29.7%.
Discussion
Hydrocortone tablets were oval in shape with a central score line. Limited disintegration occurred during halving but accurate quartering proved impossible. Tablet brittleness resulted in quarters being gathered from tablet debris; increasing the risk of under- or over-dosing. The USP limits of weight variation (85–115%) were met by the intact tablets but by only 67% of the quarters against the target 61.5 mg weight.
Conclusions
Splitting Hydrocortone tablets into quarters produced unacceptable variation in weight uniformity and HC content. Oral dosing with Corlan (2.5 mg) would be more reproducible but its pharmacokinetics taken orally are unknown. The data highlight the need for appropriate paediatric strengths and formulations of HC.

OC3.2

Adrenal function in children and adolescents with Prader–Willi syndrome attending a single centre from 1991 to 2009

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Introduction
There has recently been a suggested link between central adrenal insufficiency and the high rate of sudden death in children and adolescents with Prader–Willi syndrome (PWS). This finding has important implications for PWS management, since steroid cover could exacerbate the existing tendency towards obesity. We have retrospectively examined our data for both mortality and pituitary–adrenal axis status in subjects attending the dedicated PWS clinic at the Royal Hospital for Sick Children in Glasgow since 1991.
Methods
Case-note review of all patients in whom pituitary testing was carried out and cortisol responses to hypoglycaemia (insulin tolerance test) or synthetic ACTH recorded. A stimulated cortisol level of <500 nmol/l was considered indicative of adrenal insufficiency.
Results
Of the 69 patients who have attended the Glasgow clinic since its inception in 1991 7 have died, median (range) age of death 25.3 (14.8–40.8) years of which only one was unexpected (following pneumonia in a woman aged 40 years). Twenty-five patients (19M:6F) have undergone anterior pituitary stimulation testing, median (range) age 7.16 (0.43–16.27) years. Median (range) basal and peak cortisol were 328 (105–851) nmol/l and 915 (479–1481) nmol/l, respectively. There was no statistical difference between hypoglycaemia-induced or synacthen-induced basal ($P=0.64$) or peak values of cortisol ($P=0.72$). One patient showed a peak cortisol of 479 nmol/l in response to hypoglycaemia, while the remainder showed an adequate rise in cortisol.
Conclusion
In contrast to Roderick et al who reported an inadequate ACTH response to metyrapone in 60% of 25 patients, we found one patient with a borderline stimulated cortisol response. Given that steroids cause significant weight gain and that obesity is a major contributor to morbidity and mortality in PWS we caution against *ad hoc* steroid cover during intercurrent illness in this patient group.

OC3.3

Mutations in the *SLC29A3* gene encoding the human equilibrative nucleoside transporter-3 protein (hENT3) is associated with pigmentary hypertrichosis; insulin dependent diabetes mellitus (PHID); short stature and hypogonadism

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Background
PHID syndrome has been recently described as a unique syndrome characterised by pigmented hypertrichosis; non immune mediated insulin depended diabetes mellitus (DM). Other associated features of the syndrome include pancreatic exocrine insufficiency, short stature and hypogonadism.
Aims
To identify the genetic basis of PHID syndrome in six patients from five unrelated families and to characterise the endocrine features associated with this syndrome.
Methods
Homozygosity mapping was performed in all five families followed by candidate gene sequencing in our cohort of six patients. Functional studies were performed on the diseased fibroblasts. Combined pituitary function test was performed to assess GH and pituitary–gonadal axis in 2 patients.
Results
Homozygosity mapping identified a single common 1.4 Mb region of shared homozygosity within cytogenetic band 10q22.1. Five loss of function mutations were found in *SLC29A3* gene (three missense, one frameshift and one nonsense). Functional studies from the diseased fibroblasts revealed a 34% reduction in the hENT3 mRNA and defect in cellular trafficking of residual protein. Oral glucose tolerance test showed undetectable insulin secretion in the face of high blood glucose concentration. Investigation of short stature revealed adequate GH response to glucagon stimulation test however patients failed to generate an IGF1/BP3 response to GH treatment suggestive of GH resistance. GnRH test

revealed features of hypogonadotropic hypogonadism in a female with failure to attain puberty at 16 years of age.
Conclusion
Inactivating mutations in the human *SLC29A3* gene causes a novel Mendelian disorder associated with insulin dependent DM; pigmented hypertrichosis; short stature and hypogonadism. Mutations in *SLC29A3* lead to alterations in cell size/number possibly via the insulin signalling pathway. Further studies are required to understand the role of hENT3 protein in pancreatic endocrine and exocrine tissues and in the pituitary gland.

OC3.4

Severe midline abnormalities result in a distinct spectrum of endocrinopathies: implications for genetic diagnosis and follow-up

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Background
Holoprosencephaly (HPE) is a brain malformation that results from a defect in the patterning of the forebrain. Children with the most severe forms of HPE have endocrine deficits, in addition to neurologic and visual impairment. Forebrain abnormalities and pituitary hormone deficiencies are also part of the clinical spectrum of septo-optic dysplasia (SOD).
Aim
Describe the spectrum of endocrinopathies in children with HPE and compare their characteristics to those with severe SOD, as defined by the combination of optic nerve hypoplasia, pituitary hormone deficiencies and defects in the midline structures.
Results
Twenty-two patients with severe HPE presented to our department; we compared their characteristics to those of 28 children with severe SOD. Children with HPE presented at a mean age of 1.4 ± 1.3 years, with a mean height SDS of -2.08 ± 1.0. Diabetes insipidus (DI) was observed in 54.6%, either in isolation (18.2%) or in combination with anterior pituitary hormone deficiencies (36.4%). More than half (54.5%) were diagnosed as growth hormone deficient, 40.9% had ACTH deficiency and 18.2% had TSH deficiency. The majority of patients with HPE had an absent (56.3%) or dysplastic (25%) corpus callosum, and more than half had an absent septum pellucidum (56.3%). There was no significant difference in the appearance of the midline structures between the two groups. The incidence of DI was significantly higher in children with HPE compared to those with SOD (54.5 vs 18.5%, $P<0.05$), whilst TSH deficiency was more frequent in patients with SOD (48.1 vs 18.2%, $P<0.05$). There was no significant difference in the incidence of GHD (54.5 vs 59.3%, $P>0.05$) and ACTH deficiency (40.9 vs 59.3%, $P>0.05$) in children with HPE and SOD respectively.
Conclusions
Children with severe HPE and SOD present with a variable but distinct spectrum of pituitary hormone deficiencies. The greater involvement of hypothalamic nuclei in children with HPE may account for the increased incidence of DI.

OC3.5

Pituitary function at least 4 years after traumatic brain injury in childhood

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Introduction
Post-traumatic hypopituitarism (PTHP) is a recognised sequel of traumatic brain injury (TBI), occurring in 25–69% of adult patients, but there are few data on the prevalence or natural history in childhood. Our aim was to determine pituitary function in children at least 4 years after TBI requiring paediatric intensive care unit (PICU) admission. At the same time body composition was evaluated.
Methods
Children discharged from the regional PICU with TBI from 1999 to 2004 ($n=127$) were recruited. Clinical markers of TBI severity were obtained from case notes. Height, weight, waist circumference, and body fat percentage by skinfold thickness (SFT) and bioelectrical impedance (BIA) were measured. Blood and urine samples were collected for baseline pituitary function testing. Body composition was compared to age and sex matched controls.
Results
Eighteen patients (mean age 16.5 ± 3.8y, 16 independently mobile) agreed to participate. Age at injury (10.0 ± 4.4y) and gender (67% male) were similar to the whole cohort. Participants had longer duration of PICU admission (8.6 ± 5.5d vs 4.9 ± 6.1d, $P=0.001$) and inotropic support (4.6 ± 3.1d vs 1.5 ± 4.6d, $P<0.001$) and lower GCS on arrival (7 ± 3 vs 10 ± 4, $P=0.005$). Mean interval from injury to assessment was 6.5 ± 1.6y. Standard deviation scores for height (-0.21 ± 1.16), weight (0.21 ± 1.22) and BMI (0.35 ± 1.31) and body fat percentage (SFT 24.2 $\pm 7.1\%$; BIA $21.1 \pm 7.7\%$) were not significantly different from controls. Mean difference from mid-parental height SDS was 0.02 ± 0.80. Biochemical evidence of hypopituitarism was identified in only one case but this may have been caused by other confounding factors.
Conclusion
Pituitary dysfunction was less prevalent than published studies, despite the recruited patients having more severe injuries. However, as the time from injury to endocrine assessment was longer than previous reports, recovery of early pituitary dysfunction might have occurred.

OC3.6

Melatonin secretion in children with sleep disturbance and septo-optic dysplasia

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Introduction
A previous case-report described one individual whose significant sleep disturbance in association with septo-optic dysplasia (SOD) was corrected with melatonin administration. Subsequently a trial of melatonin treatment in children with SOD and sleep disruption has become accepted clinical practice in many centres. There are however no published data describing melatonin secretion in these individuals.
Methods
We studied six children with sleep disturbance associated with SOD (characteristics in table below), all of whom were on adequate hormonal replacement at the time of investigation. All children wore an actiwatch-mini for two weeks and were admitted to hospital for a 24 h period during which hourly measurements of serum melatonin were taken. Sleep data were analyzed in conjunction with a detailed sleep diary completed by the children's parents over the 2-week period. Ethical approval was obtained for these studies.
Results
Actigraphic studies showed reduced sleep efficiency in all children, mainly due to frequent and often prolonged night awakenings. Only one child (1) presented with a free-running sleep pattern with incremental asynchrony suggesting a non-24-h sleep–wake disorder. Melatonin profiles of all children showed a normal circadian rhythm with mean serum levels being lowest in the day (mean 56 pg/ml) and peaking overnight (mean 380 pg/ml).
Conclusions
These findings indicate that abnormalities in timing and amount of melatonin secretion do not account for the significant sleep abnormalities observed in these children, suggesting that other as yet unexplored factors are contributing to their abnormal sleep patterns.

Table 1

	Age (years)	**Sex**	**Degree visual impairment***	**Hormonal abnormalities**
1	1.27	M	Severe	GHD, TSHD, ACTHD, DI
2	6.12	M	Moderate	GHD, ACTHD
3	6.40	F	Severe	GHD, TSHD, ACTHD
4	1.62	M	Severe	GHD, TSHD, ACTHD
5	1.67	M	Moderate	GHD
6	1.67	F	Severe	GHD

Severe, some form vision (non-light reflecting); moderate, worse than 6/18.

OC3.7

Heterogeneous tissue in the thyroid fossa on ultrasound in infants with proven thyroid ectopia on isotope scan: a diagnostic trap

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Introduction
Thyroid imaging is of proven help in establishing a diagnosis of congenital hypothyroidism in newly referred infants. Radio-isotope and/or ultrasound imaging is commonly used; each has weaknesses but have complimentary strengths and thus have been used in combination in our centre since 1999. We undertook a retrospective review and analysis of ultrasound imaging in infants with proven thyroid ectopia to re-examine the diagnoses.
Patients and methods
Eighteen infants with proven thyroid ectopia on radio-isotope scanning were reassessed. Fifteen were found to have useable images. Thyroid biochemistry at the time of diagnosis was also reviewed.
Results
All infants showed the presence of tissue bilaterally in the thyroid fossa. This tissue was deemed to be non-thyroidal in nature since, apart from being non-functional on isotope scan, it exhibited some or all of the following typical features: hyperechogenicity, heterogeneity, significantly smaller size than normal neonatal thyroid ($P \leq 0.001$), poor vascularity and anechoic and/or hypoechoic cystic areas. A striking and consistent ultrasonographic finding was the extension of this tissue behind and around the great vessels of the neck – a previously unreported feature. Quantitative thyroglobulin measured at diagnosis was highly variable (2–612 μg/l) although the median value was 181.5 μg/l.
Conclusion
Considerable experience is required to interpret ultrasound data in neonates with abnormal thyroid function. We caution against diagnosing dysplastic thyroid *in situ* on the basis of ultrasound alone, particularly if the tissue exhibits any of the features we describe which are associated with non-thyroidal, cervical tissue found *in situ* in proven thyroid ectopia. A combination of initial venous thyroid function, including thyroglobulin measurement, and dual ultrasound and isotope scanning enhances diagnostic accuracy.

OC3.8

Determinants of remission and relapse in a cohort of children with thyrotoxicosis treated with dose titration of carbimazole

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Introduction
Factors determining remission and relapse in children with thyrotoxicosis include ethnicity, age and thyroid hormone levels at diagnosis. We investigated if similar factors influence remission and relapse in a contemporary cohort of children with autoimmune thyrotoxicosis treated by dose titration of carbimazole.
Methods
Forty-seven children (39 females) with thyrotoxicosis, treated with carbimazole, were followed up for ≥ 2 years. Initial remission was defined as first cessation of carbimazole and long term remission was defined if remission lasted >2 years. Relapse was defined as recommencement of carbimazole following remission or a dose increment on existing treatment.
Results
First remission was achieved in 28 (60%) children after a median (range) of 1.5 (0.3, 3.1) years after diagnosis, while long-term remission was achieved in 8 (17%). Relapse occurred in 37 (78%) children 1.9 (0.2, 6.7) years after diagnosis. Following remission, relapse occurred in 20 (71%) children, while remission after relapse was rare at 14%. Treatment with surgery or radiotherapy was given to 22 (46%) children. In survival analysis, risk of relapse was associated with a lower body mass index at diagnosis (hazard ratio (HR) (95% confidence interval) 14.5 (1.6, 126.2), $P=0.02$) and a higher dose of carbimazole 6 months after diagnosis (HR 1.17 (1.0, 1.3), $P=0.03$) but not with non-Caucasian ethnicity, younger age or high serum free thyroxine levels. In linear regression ($R^2=0.68$, $P=0.02$), time between initial remission and relapse was negatively correlated with time to achieve initial remission ($P=0.002$) and initial dose of carbimazole ($P=0.01$), when controlling for ethnicity, age, sex and weight, suggesting an association of greater disease severity with a higher risk of relapse.
Conclusion
Most children with thyrotoxicosis treated with dose titration of carbimazole relapse after remission, especially if they are thin at diagnosis and remain on high treatment doses at 6 months after diagnosis.

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OC4.1

Parahippocampal aberrations in children with GH deficiency: a diffusion tensor imaging study

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Introduction
There is a large body of evidence to suggest that the GH axis plays an important role in brain myelination. However, results from studies in humans with an abnormal GH axis have varied and therefore there remains no consensus as to whether the GH/IGF1 axis plays a significant role in neural development. No previous studies have used diffusion tensor imaging (DTI) a sensitive magnetic resonance imaging (MRI) technique for studying brain white matter tracts, to address this question.
Methods
Fifteen children (mean 8.5 years) with isolated GH deficiency (IGHD) (peak GH to provocation <6.7 μg/l (mean 4.5 μg/l) plus a pathologically low IGF1 concentration for age (mean -2 S.D. for age and sex)), and twelve children (mean 8.3 years) with isolated short stature (ISS) (peak GH to provocation >10 μg/l (mean 14 μg/l), normal IGF1 measurements and growth rate) were studied. All underwent MRI imaging of the brain (DTI sequences acquired) and a comprehensive neuropsychological assessment including the Weschler Intelligence Scale for Children (WISC-IV) and the Movement-ABC (M-ABC) test. The fractional anisotropy (FA) images were processed using tract-based spatial statistics, and automated, observer-independent, voxel-by-voxel whole-brain between-group analysis performed.
Results
Children with IGHD had significantly lower FA (reduced white matter integrity) in the parahippocampal region and temporal lobes bilaterally and performed significantly worse on the perceptual reasoning component of the WISC-IV ($P<0.05$) and the M-ABC ($P<0.009$), compared to the ISS control group.
Conclusions
These preliminary findings show that white matter abnormalities are present in specific brain regions in children with IGHD, who are impaired compared to controls in perceptual reasoning and motor performance.
Currently the main aim of GH treatment in children is to optimise final height and maintain bone mass; if GH also has a significant impact on neural development and cognition, then this may have important implications for clinical practice.

OC4.2

First report of a *de novo* heterozygous *SOX2* deletion associated with a large hypothalamo-pituitary tumour gives further insights into the role of *SOX2* in pituitary development.

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Background
SOX2 is a member of the SOX family of transcription factors (SRY-related high-mobility group (HMG) box). Heterozygous, *de novo*, loss-of-function mutations were initially reported in patients with bilateral anophthalmia/microphthalmia, developmental delay, male genital tract abnormalities, oesophageal atresia and sensorineural hearing loss. We have recently reported a number of *SOX2* mutations in patients with anterior pituitary hypoplasia and hypogonadotrophic hypogonadism. Additional features included the association with hypothalamic hamartoma and variable defects affecting the corpus callosum and mesial temporal structures. We herein report the first patient with a heterozygous *SOX2* gene deletion associated with a large hypothalamo-pituitary tumour.

Report
The proband is a female patient of non consanguineous parents who presented at the age of 18 years with pubertal delay. She had extreme microphthalmia, delayed motor milestones and severely impaired language development. At the age of 18 years, she had a height of −3.12 SDS, with a normal IGF1 (270.7 ng/ml) and GH concentration. Cortisol profile, thyroid function tests and prolactin were normal. Hypogonadotrophic hypogonadism was diagnosed with a flat LH and FSH response to GnRH stimulation. Brain MRI demonstrated a large cystic tumour consistent with a craniopharyngioma, extending into the suprasellar region. However, at the age of 24 years, she progressed to develop spontaneous but incomplete pubertal development, without change on sequential MR imaging over time. Multiple ligation probe analysis (MLPA) revealed that the patient was heterozygous for a complete *SOX2* deletion.
Conclusion
Heterozygous *SOX2* mutations are associated with hypogonadotrophic hypogonadism and anterior pituitary hypoplasia. We now describe loss of function of *SOX2* associated with a cystic mass suggestive of a craniopharyngioma. *In vitro SOX2* represses β-catenin-TCF mediated transcription. Since β-catenin overactivation has been associated with craniopharyngiomas, the *SOX2* deletion could be associated with β-catenin gain of function. The case of this patient gives further insight in the role of *SOX2* in pituitary development and tumorigenesis.

OC4.3

Pituitary adenomas presenting in children and young people: a single centre experience

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Introduction
Pituitary adenomas are uncommon in childhood and adolescence and knowledge of long-term outcomes is sparse. We describe a large cohort of patients, now attending our adult clinic.
Patients and methods
Retrospective review of patients aged ≤18 years at diagnosis of a pituitary adenoma.
Results
There were 24 patients (18 female), mean age at diagnosis 15.6 (range 11–18) years, current age 25.5 (14–47). Of 14 were prolactinomas (10 macroprolactinomas), 3 non-functioning adenomas (2 macroadenomas), 5 Cushing's disease, 1 pituitary cyst and 1 pituitary apoplexy. Of the 14 prolactinomas (all female, mean age at diagnosis 16.3 years, mean prolactin at diagnosis 12 258 (1276–60 000) mU/l), all received dopamine agonists (DA); 2 required surgery because of worsening visual field defects. One presented with short stature and delayed puberty; 5 had galactorrhoea; 12 oligo-/amenorrhoea. Current age 25.1 (16–37), mean prolactin on DA 1083 (2–5527) mU/l. Three patients have conceived spontaneously, two have been treated for infertility. Mean body mass index (BMI) at diagnosis 27.6 kg/m^2 (SDS 1.1), current BMI 34.4. Five patients with Cushing's disease underwent surgery; two relapsed and required further surgery and one radiotherapy. Of the 24 patients, the majority receive endocrine replacement (11 GH). BMI increased from 26.4 (at diagnosis) to 30.2 at latest follow-up, excluding Cushing's patients. Mean cholesterol 5.5 (3.2–8) mmol/l, one treated with a statin, one has hypertension and 2 receive orlistat.
Conclusions
This is one of the largest single centre reviews of patients aged 18 or younger when diagnosed with a pituitary tumour. Nearly 60% were prolactinomas, all occurring in females. All were treated with DA but two required surgery. Non-functioning adenomas and Cushing's are less common with no acromegaly. Increased cardiovascular risk factors (obesity and dyslipidaemia) and infertility are frequent sequelae and their active treatment is important.

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OC5.1

Specialist nurse delivered emergency telephone service for children with type 1 diabetes

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Aim
To evaluate the paediatric specialist diabetes nurse (PDSN) delivered 24 h emergency telephone contact service for families with children and young people with type 1 diabetes within Hull and East Yorkshire Hospitals NHS Trust.
Methods
A prospective audit of telephone calls received by the 2 PDSNs over a 15-month period between 1 July 2005 and 30 September 2006 for out of hours advice. All the phone calls were logged into a database and details of type of inquiry, time and duration of phone call, advice given and outcome were recorded. A questionnaire about the use of this service was sent out to parents which included a satisfaction rating about their experience of this service.
Results
During the study period total number of children and young people with type 1 diabetes within our service was 220. Of 357 telephone calls were logged. 241 calls (68%) were made between 1700 and 2100 h. 250 calls (70%) lasted ten minutes or less in duration. The topics of discussion were intercurrent illness (32%), hyperglycaemia (19%), hypoglycaemia (13%), Insulin dose adjustment (13%) and miscellaneous (23%). There were 20 admissions to the hospital following a telephone contact during the audit period (6% of the total phone calls). Of 95 questionnaires out of the 110 posted out were returned (86%). 75% of the families and young people who filled the questionnaire had used the emergency telephone contact. All the parents and young people contacting the PDSNs were either satisfied or very satisfied with the advice given.
Conclusion
A well established PDSN delivered emergency telephone service can improve patient/parent satisfaction and reduce the number of hospital contacts for families with children and young people with type 1 diabetes.

OC5.2

Survey on facilities in the local schools for children with type I diabetes (T1D)

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Introduction
Optimising management of diabetes in school is critical especially with more children being commenced on intensive insulin regimens. Partnership between families, school and caregivers is essential to enhance safety and satisfaction with the educational experience for students.
Methodology
We gathered information on facilities in schools for children with T1D from our district hospital by telephonic questionnaire. The questions related to presence or not of a designated area at school for blood sugar monitoring (BSM), insulin administration (IA) and personnel present for supervision of IA.
Results
We have 78 school children with T1D aged 5–16 years. 30 children attending 25 primary schools (PS) and 48 attending 23 secondary school (SS); 4 on twice daily injection, 1 on thrice daily regimen, 68 on basal bolus regimen and 5 on CSII. We obtained information on 33 schools and 61 children (23 in PS and 38 in SS). All children had individual care plans.
Of 30% (7/23) of children in PS and 1/38 in SS could not self-inject. Of these, Noon injection was done by parents in 7 cases and school staff in 1 case. All 33 schools had assigned rooms for BSM and IA. This consisted of medical room (21), office (7), injection room (4) and staff room (1).
All children in PS were supervised during IA by a variety of staff including first aid providers (9), teacher or assistants (7), administrative staff (7), school nurse (1) and parent (2) whilst in 11/14 of SS, supervision was present and by school nurses (7), first aiders (6) administrative staff (2) and teacher (1).
Conclusion
Facilities for children with diabetes in school is improving however, support for children who cannot self-inject is mainly provided by parents rather than school staff. Work still needs to be done to address local policies, funding for training to optimise this care.

OC5.3

Young persons' weight management service: a service users' evaluation

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Background
Obese young people are likely to suffer significant morbidity in adult life. Successful intervention during adolescence may have far-reaching benefits.

Evidence is emerging that patient-responsive clinical services may deliver improved outcomes.
Aims
To assess the perceptions of obese young people about weight and weight-management services.
Method
Annonymised, postal questionnaire survey of 116 obese young people (9–20 years), who had attended a clinic and/ or participated in obesity research at our centre. Data was analysed using SPSS.
Results
Forty-four questionnaires were returned (38%). Respondent percentages are reported. 98, 75 and 75%, respectively, 'agreed' or 'strongly agreed' that they were motivated to lose weight, change eating and exercise habits. 91, 68 and 75%, respectively, were 'likely' or 'very likely' to go walking, attend a gym or participate in exercise with similar young people. Of 51 and 47%, respectively, reported 'always' feeling anxious or sad about their weight. Of 53 and 32%, respectively, 'agreed' or 'strongly agreed' that their weight affected their sports activities and social life. Perceived causes for obesity were eating habits (22%), lack of exercise (20%), family history (14%) and stress (11%). 71 and 82%, respectively, 'agreed' or 'strongly agreed' that their obesity affects their current health and will affect their adult health.
Motivation to lose weight was correlated with impact on friendships and social activities ($r=0.4, 0.3$, respectively, $P<0.05$) and with impact on sports activities, sadness and anxiety about weight ($r=0.5, 0.4, 0.6$, respectively, $P<0.01$). There was no correlation between motivation and perceived impact upon health.
Young people would like to receive information from a personal trainer (59%), dietician (54%) doctor (43%), group discussion (40%). The most popular information delivery formats were leaflets (42%) and website (40%).
Conclusions
An adolescent weight-management service incorporating personal mentors, peer support and website may harness motivation more successfully than the conventional medical model.

OC5.4

Diabetes mellitus and hyperinsulinaemic hypoglycaemia (HH) due to dominant ABCC8/KCNJ11 mutations

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Background
The pancreatic β-cell K_{ATP} channel plays a key role in glucose stimulated insulin secretion and is encoded by the genes *ABCC8* and *KCNJ11*. Recessive mutations in *ABCC8/KCNJ11* cause severe medically unresponsive HH. Recently, dominant mutations in these genes have been described that cause mild, medically responsive HH. Controversy exists on whether these dominant *ABCC8/KCNJ11* mutations predispose to diabetes mellitus in adulthood or not.
Aim
To characterise the phenotype of the dominantly inherited *ABCC8/KCNJ11* mutations causing HH and study the prevalence of diabetes mellitus in the adult mutation carriers.
Methods
We studied the phenotype of ten families (fourteen patients with HH) with nine different dominant *ABCC8/KCNJ11* mutations. Functional consequences of six novel mutations were examined by reconstituting the K_{ATP} channel in HEK293 cells and evaluating the effect of drugs (diazoxide, glibenclamide) and metabolic poisoning on the channels using Rb^{86} flux assay.
Results
HH was diagnosed at a median age of 1 day. The median birth weight was 4303 g at a median gestational age of 40 weeks. 12/14 probands responded to diazoxide, while the remaining two had transient HH that resolved spontaneously. Of the sixteen adult mutation carriers identified, only five have persisting or past symptoms of hypoglycaemia. Five adult mutation carriers have developed young onset diabetes mellitus, at a median age of 38 years whilst three others have developed gestational diabetes. When activated, wild-type K_{ATP} channels showed significant Rb+ efflux whereas mutant K_{ATP} channels showed no Rb+ efflux thus confirming the pathogenicity of the mutations.
Conclusions
Dominant mutations in *ABCC8/KCNJ11* cause a varying phenotype ranging from asymptomatic macrosomia to medically responsive HH in childhood. In adults, it may be an important cause of dominantly inherited early onset diabetes mellitus.

OC5.5

Point of care blood ketone level: a useful tool to diagnose DKA?

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Background
ISPAD clinical practice consensus guidelines 2006–7 defined DKA as: blood glucose >11 mmol/l in presence of venous pH <7.3 or bicarbonate <15 mmol/l, ketonaemia and ketonuria. The level of ketonaemia or ketonuria was not specified. Blood ketones can be checked easily using a blood ketone meter (Optium). In our institution we have been measuring them on all children admitted with suspected DKA over the last 5 years. A blood ketone level of >3.0 mmol/l was considered as frank ketoacidosis.
Aim
To determine if blood ketone levels at admission correlate with traditional methods of diagnosing DKA (pH, bicarbonate and blood glucose), and whether they usefully aid the diagnosis.
Method
Retrospective data were collected on all children under the age of 16 years who were hospitalised with DKA at our institution over a 3 year period (2006–8). Admission data recorded were: blood ketone levels; venous pH; serum bicarbonate and blood glucose levels.
Results
Sixty-three episodes of DKA were scrutinised in 51 patients. Of 44/63 (70%) had ketone values >3.8. 32/44 (73%) cases corresponded to blood pH <7.3 and bicarbonate <15 mmol/l. There was no relationship between blood ketone and glucose levels ($r=0.12$, $P=0.35$); however there was a significant negative relationship between blood ketones and pH ($r=-0.425$, $P=0.001$) and between blood ketones and serum bicarbonate ($r=-0.594$, $P<0.001$) which indicates that the higher the blood ketones, the lower the pH and bicarbonate levels.
Conclusions
Blood ketone levels may be a useful tool to aid the diagnosis of DKA. Ketone levels >3.8 should prompt urgent medical assessment. Further large prospective studies are required to assess the reliability of the correlation between ketonaemia and acidosis.

OC5.6

Ongoing benefit of CSII in the improvement of HbAlc and BMI in a cohort of children with type I diabetes

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Introduction
Tight metabolic control reduces the risk of microvascular complications in individuals with type 1 diabetes (T1DM). Multiple studies have shown improvements in quality of life (QOL) in children following the introduction of continuous subcutaneous insulin infusion (CSII) but metabolic outcomes have been more variable. This audit looked at metabolic parameters at long-term follow up in children and adolescents using CSII over 3 years.
Methods
Fifty-seven children and adolescents are using CSII therapy in our unit with greater than one year follow up post pump initiation available for 45 patients (median age 14.2 years, twenty-three males). Data was collected prospectively on all children on HbAlc, incidence of severe hypoglycaemia and diabetic ketoacidosis, as well as anthropometric data.
Results
The median duration of diabetes was 7.4 years (range 1–19.2 years), median duration using CSII was 2.7 years (range 1–4.5 years). Mean HbAlc decreased from 8.9% at commencement to 8.1% at 1 year ($n=45$, $P<0.001$), 8.1% at 2 years ($n=36$, $P<0.001$) and continued to decrease to 7.9% at 3 years ($n=23$, $P<0.001$) post pump initiation. Mean BMI z-score remained stable throughout the follow up period. There were thirteen severe hypoglycaemic episodes documented in this cohort in the year prior to pump commencement compared to one episode (due to an accidental insulin overdose) in the three years of follow up. The incidence of DKA was low but fell further during pump therapy (two episodes in the year prior to pump therapy versus two episodes in 3 years of follow up).
Conclusion
Continuous subcutaneous insulin infusion therapy is safe and effective in children and adolescents and is associated with sustained improvements in metabolic control and reductions in adverse outcomes without negative impacts on BMI.

Oral Communications 6

OC6.1

Rising incidence of type 1 diabetes mellitus in children and adolescents under 15 years in the Republic of Ireland in 2008 (Preliminary figures)

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Background
The incidence of type 1 diabetes mellitus is increasing worldwide with recent European data suggesting annual increases ranging from 0.6 to 9.3%, the overall rate being 3.9%. It was thought that the Republic of Ireland (ROI) had one of the lowest disease incidences in Europe. The first Irish study of T1DM incidence which provided a measure of case ascertainment, confirmed a high incidence rate (IR) at 16.6 per 100 000 placing this population, in the upper quartile of disease incidence.
Objectives
To determine the incidence of type 1 diabetes in children and adolescents <15 years in ROI in 2008 and to establish a National Diabetes Register. To confirm the status of ROI as an area of high disease incidence, and ascertain if the incidence has increased. To act as the base year for the National Register.
Methods
Prospective national reporting of incident cases of type 1 diabetes <15 years as a primary diagnosis by Paediatricians and Paediatric Endocrinologists nationally was undertaken from January 2008. Following informed consent of children and parents further information was obtained using a standardised dataset. Completeness of ascertainment was assessed using the capture-recapture methodology. Intercensal estimates were used for calculation of (IR).
Results
Preliminary figures for 2008 indicate that the (IR) of T1DM within this population has increased an average of 6% per annum since 1997. This increase is across all age groups but most marked in boys aged 10–15 years and boys under 5 years.
Conclusions
Initial data verifies a high and rising incidence of T1DM in Irish Children supporting the need for epidemiological monitoring in this population. A national diabetes register is vital to monitor changes in disease incidence, and provide important epidemiological and robust denominator data for clinical audit. It is essential to inform resource allocation decisions in this important disease.

OC6.2

Microalbuminuria screening on type 1 diabetes

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Introduction
Microalbuminuria is the first of sign of incipient nephropathy and other micro vascular complications in the diabetic population. Up to 30% of the paediatric diabetic population are at risk of developing microalbuminuria by the age of 20. NICE 2006 recommends microalbuminuria screening from 12 years of age in children with type 1 diabetes however there is no guidance on specimen collection, test methodology or treatment regime. The definition ofmicroalbuminuria varies with type of specimen and test offered resulting in different screening practice in different hospitals in the UK.
Method
A postal questionnaire was sent to 100 paediatric diabetic services in the United Kingdom. The questionnaire asked the age of commencing microalbuminuria screening, the collection procedure, specimen numbers, methodology of microalbuminuria test and criteria for repeating the specimen and initiation of treatment for abnormal results.
Results
The response rate was 61 with 90% of hospitals screening for microalbuminuria annually, 33% units screening 5 years after diagnosis. Of 70% of hospitals commenced screening before 12 years of age. Of 65% undertook microalbumnuria screening on early morning urine and 94% used the albumin cretatinine ratio and there is wide variation in repeating the specimen for abnormal results. Nephrology referral occurred for persistent microalbuminuria for more than 6months in 31% units and more than 12 months in 57% units. Of 50% hospitals would consider starting ACE inhibitors.
Conclusion
The majority of respondents undertook microalbuminuria screening but only 30% follow nice guidance. There is wide variation in screening practice on method, type of specimen, repeating test on abnormal results and also seeking advice from Nephrologists. Detailed studies are required to ensure a National consensus on microalbuminuria screening, methodology and ongoing management for the paediatric diabetic patients.

OC6.3

Audit of paediatric diabetic eye screening

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Introduction
NICE recommends annual screening for diabetic retinopathy in children with type 1 diabetes aged over 12 years and/or with duration of diabetes over 5 years. This audit aimed to evaluate patient attendance for retinopathy screening, to identify the prevalence of retinopathy and maculopathy and to ascertain characteristics of patients.
Methods
This was a retrospective audit of patients attending for eye screening from January 2008 to April 2009, in a large paediatric diabetic clinic ($n=329$). Data from the Twinkle database was used to identify patient attendance, socio-demographic information, HbAlc, duration of diabetes and microalbuminuria. Patients with retinopathy were compared to those without retinopathy.
Results
Of 145 /189 (89%) eligible patients attended screening, median (range) for age 13.5 (7.1–18.2) years, duration of diabetes 6.0 (0.5–13.8) years, and HbAlc 8.9 (5.8–14)%. Of 29/145 (20%) patients had stage one retinopathy (one or more haemorrhage and/or microaneurysms). Patients with retinopathy had a significantly higher HbAlc (9.9 vs 8.7%), longer duration of diabetes (8.1 vs 5.5 years) and higher microalbuminuria (10.1 vs 7.1 mg/mmol), (all $P<0.05$). There was no significant relationship of retinopathy to age.
Conclusion
There are significant differences in metabolic control in children with or without early retinopathy. Diabetic retinopathy is a common finding even within a paediatric clinic. Feedback of results to patients can be used as a motivational factor to improve glycaemic control. The significant rate of microvascular complications in this paediatric cohort stresses the urgent need to implement alternative strategies to improve glycaemic control with the goal to reduce long-term morbidity and mortality.

Poster Presentations

P1

Lipoatrophy with insulin analogues in four children with type 1 diabetes

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Introduction
Lipoatrophy (LA) was common before the advent of recombinant human insulin. More recently, insulin analogues have been widely introduced into paediatric practice. In the literature, LA has only been reported so far with insulin Lispro (Lily, USA) ($n=4$ adult patients and 3 children) and insulin Glargine (Sanofi-Aventis, France) ($n=1$ adult patient). To our knowledge; this is the first report of LA with insulin Aspart (NovoRapid), biphasic insulin Aspart (Novomix 30) and insulin Detemir (Levemir) (Novo Nordisk, Denmark).
Case reports
Four children with type 1 diabetes were commenced on Novomix 30 ($n=2$) or Novorapid/Levemir injections ($n=2$). They developed LA at the injection sites after 2–3 years. One patient developed LA at the Novorapid site and the other at the Levemir site. The mean HbA1C ranged from 8.0–9.9%. Insulin antibody levels were high in 3/4. In 2/4, LA resolved by changing the injection site. It recurred at the new sites in 2 but resolved after changing the insulin preparation (Novomix 30 to Humalog mix25 and Levemir to insulin Glargine). HbA1C had steadily dropped to 7.4% along with the resolution of LA in one patient. LA resolved over a period of 1–2 years in all patients.
Discussion
The pathogenesis of LA is poorly understood. The suggested mechanisms are: repeated mechanical trauma from the injections, cryotrauma from refrigerated insulin or immune mediated. In 2/4, LA resolved after changing the injection site suggesting that local factors could be the cause of LA. It is our practice to examine the injection sites on each visit and this facilitated early detection of LA.
Conclusion
LA is a rare complication of treatment with insulin analogues. It may be sufficient to change the injection site to manage LA. If that is not effective, changing to an alternative analogue was successful in our experience.

P2

Scopes and Barriers for management of childhood obesity

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Objective
The aim of our study is to evaluate the current practice, resources available and barriers to primary and secondary professionals providing care for children who are overweight or obese.
Methods
A questionnaire was sent to primary and secondary care providers including General Practitioners (GP), Practice Nurses (PN), Health visitors, school nurses and community nurses in a selected Primary Care Trust and hospital doctors in Pennine Acute Trust Hospitals.
Results
Ninety-Seven (40%) professionals replied. Height and weight was routinely measured by 96% of Paediatricians verses only 42.5% of Primary Care workers; Body Mass Index was calculated by 65% and 27% respectively.
More than half the professionals (82%) followed-up patients solely within their own setting. Satisfaction scoring (out of 5) relating to ability to provide help and support to obese children were generally low especially with respect to training (1.88), self expertise (2.5), exercise programmes (1.88), family acceptance (2.22) and engagement (2.4). 15% and 3% of respondents referred to Dietitian and Psychology services respectively.
Only 70% of Senior Paediatricians and GPs were aware of NICE guideline. With respect to service availability 14% respondents were not aware of the local services, 32% had a dietitian service, 5% psychology access and only 10% had local exercise programme availability.
Conclusions
In spite of extensive campaigning by the government and the NICE guidelines, this study identified shortfalls and dissatisfaction in training, assessment, management and services available to help children with obesity. Improved training, assessment, service provision and collaborative working are needed between healthcare and non-healthcare services to help tackle Childhood obesity, an increasing epidemic with high morbidity and mortality.

P3

Abstract withdrawn.

P4

Use of clinic proforma as a tool has been shown to improve diabetic reviews

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Acute and long-term complications attributable to diabetes are regrettably still common. To monitor for the development of such complications NICE recommend regular measurement of certain criteria to enable early intervention. A previous audit performed in our hospital looked at the adherence of paediatric diabetic reviews to NICE guidelines. As a consequence of this audit a detailed pro-forma to be used at all paediatric diabetic reviews was introduced.
This poster presents the results of a closed loop audit that has resulted in our service offering improved clinical care. Patients were selected randomly from a local database of paediatric diabetic patients and the notes reviewed retrospectively for evidence of meeting the NICE criteria.
It was found that thyroid and coeliac screening improved to 100% from an initial 86% and 87.5% respectively. Improvement was also noted in the documentation of foot reviews (up 29% from 0%), growth charting at every visit (up 40% to 50%) and blood pressure monitoring (up 50% to 75%).
The pro-forma allows individual targeted changes to be made or added with ease if areas for improvement are identified during the audit process. In this last audit it was identified that dental reviews continued to be poorly documented and therefore a designated space to document these has now been included; this will hopefully trigger a similar level of improvement as shown in other areas over the last year.
Other changes included a tick box for "growth chart plotted" and a line to state definitively whether microalbuminuria was present on urine dip (rather than just whether urine was checked).
In conclusion the introduction and use of a pro-forma can facilitate an improvement in the care of paediatric diabetic patients working toward standardised national targets. The resultant pro-forma has the potential to be used at a national level.

P5

Hyponatremia in Type 1 Diabetes: Pseudohyponatremia or presentation of autoimmune Adrenal Dysfunction

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Autoimmune destruction of adrenal gland is rare in the paediatric population and can present in type 1 diabetic mellitus (TIDM). Patients with TIDM are routinely screened for Autoimmune hypothyroidism and coeliac disease. We would like to present an unusual case of hyponatremia in patient with TIDM due to simultaneous developments of both glucocorticoid and mineralocorticoid deficiency.
Fourteen-year-old Type 1 Diabetic male presented with incidental persistent hyponatremia. He was clinically well and had poor diabetes control with few hypoglycaemic episodes. There was strong family history of autoimmune thyroid disorder. He had significant urinary losses of Sodium. He had a Suboptimal incremental rise in cortisol levels on short synacthen test. His Thyroid function test was normal.He had a markedly raised Adreno-corticotrophin hormone level (3172 pmol/l, Normal Range: 10–60)and also had positive anti adrenal antibodies. CT Scan of adrenal gland was normal. Oral Hydrocortisone only made minimal difference to plasma sodium levels and addition of fludrocortisone (50 Micrograms) normalised his plasma sodium
There have been recent genetic studies identifying a gene which confers risk for auto-immune Addison's disease and Type 1 Diabetes. The occurence of multiple organ specific autoimmune disorders in the same patient have been well documented.It is therefore important to have a low threshold to investigate diabetic patients with hyponatremia and not to dismiss this an pseudohyponatremia

P6

Growth, Final Height and Endocrine Sequelae post Bone Marrow Transplantation in a UK population of patients with Hurler Syndrome (MPS 1H)

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Introduction
Hurler Syndrome, (MPS1H) is an inborn error of metabolism which was previously fatal in childhood. Bone marrow transplantation (BMT) has transformed the prognosis for these children. First BMTs are preconditioned with chemotherapy, and we have therefore put in place surveillance for endocrine sequelae. We present for the first time data on final adult height in children with MPS 1H post BMT, as well as the endocrine complications seen in this cohort.
Methodology
Retrospective case note study and a prospective programme of growth and endocrine assessment.
Results
Twenty-two patients were eligible for inclusion, mean age at last assessment 12.2 (Range 6.2–21.6) years. Age at BMT 1.3 (S.D. 0.6) years. Conditioning for first BMT included busulphan and cyclophosphamide with 5 out of 10 second transplants receiving total body irradiation. Height SDS showed a progressive fall over time. Final height (FH) was attained in 7 patients: Male FH SDS -4.8 (S.D. 0.9), Female FH SDS -3.8 (S.D. 1.3). Assessment of the GH-IGF axis was undertaken in 13: 9 had evidence of GH resistance, 1 had GH deficiency. Adrenal and thyroid function was normal in all. 11 patients were peri or post pubertal. 2 females had pubertal failure requiring intervention, with raised gonadotrophins. All male patients had spontaneous, normally timed complete puberty; however 2 post pubertal patients have reduced testicular volumes implying germinal cell damage. Most importantly insulin-glucose status has been monitored with OGT testing. 5 out of 13 tested had an abnormality of glucose metabolism.
Conclusion
Growth is impaired in this cohort primarily related to progressive skeletal dysplasia, but also associated with GH resistance. Full pubertal development may be compromised and abnormalities of glucose metabolism are common. We recommend endocrine surveillance for these patients.

P7

Increased Hypothalamic-pituitary-adrenal axis (HPAA) activity after childhood bone marrow transplantation (BMT) with total body irradiation (TBI) results in chronic hypercortisolaemia associated with obesity

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Introduction
Data on the impact of TBI on the HPAA are limited. This study investigates the HPAA in BMT-survivors and non-BMT controls using overnight serum cortisol profiles and midnight/9am ACTH levels.
Subjects ($N=35$)
$N=14$, child (7), adult (7) controls, $N=21$ child (7), adult (14) BMT-survivors (TBI dose 12.0-14.4Gy). None had had treatment with corticosteroids in the last year.
Method
Subjects rested for 3 h after venous cannulation, then blood samples were taken every 20 min between 9pm–9am. Subjects slept at their usual time and waking time was recorded. Body composition was measured by DEXA. Cortisol profiles were analysed using Cluster and Autodeconvolution software.
Results
Median (range) age at and time since BMT were 5.8 (0.2–16.0) yrs and 3.5 (1.2–19.3) yrs respectively. Peak cortisol was higher in BMT-survivors (183 vs 143 nmol/l, $P=0.048$) and in females compared to males across the groups (215 vs 138 nmol/l, $P<0.000$). % body fat was also higher in females (36.7 vs 24.3, $P=0.003$) and correlated with area under the curve (AUC) ($r=0.335$, $P=0.05$) and peak cortisol ($r=0.467$, $P=0.005$). Covariate analysis showed female gender was the main determinant of peak cortisol ($P=0.002$). Trough cortisol levels (AUC 9-11.40pm) were higher in BMT-survivors (75.4 vs 26.9 nmol/l/min, $P<0.05$) and females versus males (83.0 vs 40.0 nmol/l/min, $P<0.05$). Covariate analysis identified BMT as the main determinant of trough levels ($P<0.05$). There was no difference in time of awakening, CAR, AUC, time of peak, or ACTH levels between BMT-survivors and controls. Time from BMT correlated with trough cortisol levels ($r=0.478$, $P=0.03$).
Discussion
Therefore age, gender, adiposity and BMT all influenced HPAA activity. Gender and adiposity were pre-eminent factors for peak cortisol whereas BMT influenced raised trough levels. This may relate to TBI or to chronic stress altering HPAA feedback regulation.

P8

The Current UK Experience of Recombinant IGF1 For Cases of Severe Primary IGF1 Deficiency

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Background
Severe primary IGF1 deficiency (SPIGFD) is defined in children as a height less than −3sds, low IGF1 levels with normal growth hormone levels. Recombinant IGF1 (rhIGF1, Mecasermin) given twice daily as a subcutaneous injection is the only therapy available to improve the height potential in this group of children. However it may have important side effects including hypoglycaemia, growth of lymphoid tissue and injection site lipohypertrophy.
Aim
To accumulate the UK experience in implementing and monitoring therapy with rhIGF1 and to report short term data on response to treatment. The data from 5 centres (representing 6 of the 7 children on rhIGF1 for SPIGFD in the UK) was collected by a standardised questionnaire.
Results
All 6 children were of South Asian origin. The duration of treatment has ranged from 0 to 2 years (median 0.2 years). The starting dose was 0.04 mg/kg bd; the interval between dose increases was 1 week to 6 months. 2 children have reached the upper dose limit of 0.12 mg/kg bd. Treatment was commenced in hospital in 4 children and blood sugars were mainly monitored at initiation and dose adjustments. 1 child had a reported hypoglycaemia one year into treatment. Injection site hypertrophy or pain was the most common reported adverse event (4 children).
The median age of starting treatment was 10.6 years (range 6,11.7 years). The median height sds in the 5 children with post treatment measurements has increased from −5.3 to −5.1sds.
Conclusion
Recombinant IGF1 therapy appears to be well tolerated in the short term with most adverse events involving the injection sites. There are some early improvements in the height sds and scope for further dose increases still remain. Longer term monitoring remains essential to provide a safety profile and to assess clinical benefits.

P9

Improvement in growth of children with crohn's disease following anti-TNFα therapy can be independent of pubertal progress and glucocorticoid reduction

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Introduction
Treatment with anti-TNFα therapy such as infliximab may improve growth in children with CD but the extent of improvement in growth and its relationship to pubertal progress and changes in glucocorticoid therapy are unclear.
Aim
A retrospective study of growth, puberty and disease activity over the 6 months prior (T-6) to starting infliximab, at baseline (T0) and for the following 6 months (T+6) in CD. Results are expressed as median(10th, 90th).
Subjects & Methods
The growth and treatment details of 28 children (M:17) who were started on infliximab at a median (10th, 90th) age of 13.1yr(10.0,15.7) were reviewed. In 20 children, pubertal data were also available at all time points. Data on disease

markers (CRP, ESR, and Albumin),total Alkaline Phosphatase (ALP) and a physician global assessment were also collected.
Results
Out of 28 cases, 21(75%) demonstrated a clinical response to infliximab treatment. Overall, height velocity(HV) increased from 3.6 cm/year (0.4, 7.8) at T0 to 5.5 cm/year (2.1, 9.2) at T+6 ($P=0.003$). In infliximab responders, HV increased from 1.9 cm/year (0.3, 7.1) to 6 cm/year (2.3, 9.1) ($P=0.003$) and in the non-responders, HV remained static at 4.3 cm/year (2.5, 8.6) at T0 and 3.0 cm/year (2.0, 11.3) (NS) at T+6. HV also increased in the subgroup of 13 children who had remained prepubertal from 4.5 cm/year (0.4, 8) to 5.5 cm/year (3.3, 8.4) ($P=0.05$). In the subgroup of 11 children who had a reduction (n, 2) or cessation in GC (n, 9), HV increased from 1.8 cm/yr (0.3, 8.3) at T0 to 5.6 cm/year (2.2, 9.2) at T+6 (NS),whereas those children who did not receive GC over the12 months had an increase from 3.7 cm/year (0.6, 6.5) to 6.4 cm/yr (2.9, 9.0) ($P<0.05$). HV at T0 and T+6 showed a significant association with the average ALP over the prior 6 months (r, 0.39, $P<0.05$). HV didn't show any association with individual markers of disease activity.
Conclusion
Clinical response to infliximab therapy is associated with an improvement in linear growth in children with CD.This increase is also seen in prepubertal and GC naïve children and cannot solely be attributed to a change in these factors.

P10

Defining Criteria for Poor Responders to Growth Hormone (GH) in Short Children Born Small for Gestational Age (SGA)
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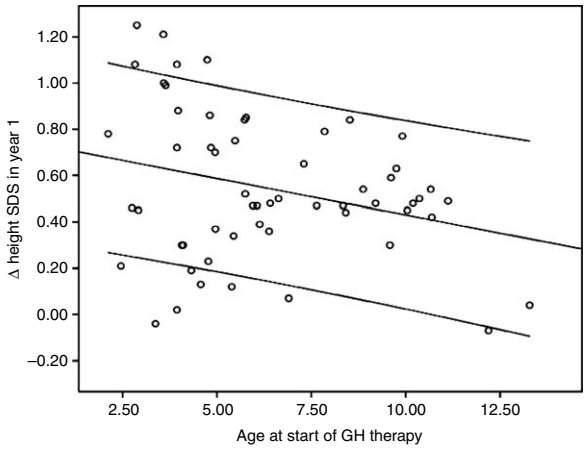
An estimated 5% of all newborns are born SGA (weight less than -2SD at birth), with 10% failing to catch up and becoming eligible for GH treatment. Not all children respond to GH, but the criteria for determining a non-responder have not been clearly defined. We have therefore evaluated first year growth performance of short SGA children treated with GH in The Growth Clinic, Manchester. Clinical and auxological data were collected retrospectively from the case records of 57 SGA patients. In our cohort, regression analysis identified starting GH dose as the most significant variable influencing first year growth response ($R^2=7.2\%$, $P=0.06$). Age also influenced response (see figure). The lower line of the figure approximately represents the 10th percentile. We propose that a height SDS increment below this line represents a clinically insignificant response (e.g. Δheight SDS $<$ 0.2 for a child age 5).



It is important to define what is an acceptable treatment response at the initiation of GH, so that decisions can be made promptly to discontinue GH and/or consider alternative treatments.
Figure: Relationship between first-year growth performance and age. Regression line with 80% confidence intervals shown.

P11

Evaluation of an automated bone age scoring program against a single observer, using the TW3 scoring system
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Background
Bone age assessment is used in the management and monitoring of treatment effects in growth disorders. This may be associated with a considerable variability between reporters. This subjectivity has raised questions about acceptable levels of error in our current practice and has led us to search for other tools for assessing bone ages.
Method
A single observer was trained in reporting bone ages using Tanner Whitehouse 3 atlas and these results were compared to an automated bone age scoring system (BonExpert).
Results
Currently this study includes 42 patients (21 male) with an age range of 7.1 to 16.4 years, who have had bone age assessments undertaken for clinical indications.
The mean (S.D.) decimal age of the group was 11.6 years (3.7). The mean difference between the single observer and BonExpert was −0.03 years (0.71). The mean percentage difference is 0.02% (6.2%). Overall 5 bone ages had a difference of greater than 1 year between the manual and automated scoring systems.
Conclusion
An automated bone age scoring system may be a reliable and reproducible method to score bone ages utilising the TW3 system.

P12

The IGF system during acute hypoxia in children
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The hypoxia, associated to intra-uterine growth restriction, is related to high concentrations of IGFBP1 and unchanged concentrations of IGF1 in animals. Nevertheless, during threatening life events, low IGFI concentrations and high IGFBP1 concentrations was reported. Furthermore, severe hypoxia increased the IGF1R expression of the neuronal growth cones in the ovine fetal brain. No information is available regarding the regulation of the IGF system by the acute hypoxia in humans. The aim of this study was to evaluate the effect of acute hypoxia on the IGF system in children. Twenty seven previously health children (14 boys and 13 girls) aged 15 days to 9.5 years were studied in 2 different situations: during acute hypoxia due to acute respiratory distress and after full recovering. In these two opportunities oxygen saturation was accessed using pulse-oximeter and blood samples were collected for serum IGF1 and IGFBP1 determination and also for analyzing of IGF1R gene expression in peripheral lymphocytes. IGF1 and IGFBP1 were determined by specific ELISA. Lymphocytes were first isolated from other blood cells using Fycoll-Hypaque and then RNA was extracted. The levels of mRNA expression of the IGF1R gene were analyzed by quantitative real-time PCR. Data were pared-compared by Wilcoxon non-parametric test. Oxygen saturation was $87.8\pm3.5\%$ in the fist evaluation (Hypoxic state or HS) and $96.4\pm1.2\%$ after recovering (non-HS) ($P<0.0001$). IGF1 levels were lower during HS compared to non-HS (median: 12 vs. 56 ng/ml) ($P<0.0001$) whilst IGFBP1 were higher during HS than in non-HS (median: 113 vs. 60 ng/ml) ($P=0.004$). The expression of IGF1R mRNA, expressed as $2^{-\Delta\Delta C_T}$, were higher during HS than after it (1.28 vs 0.93) ($P=0.03$). In conclusion, the above results showed during acute hypoxia a combination of alterations usually associated with decrease of IGF action. The higher expression of IGF1R mRNA may reflect an up regulation of the transcriptional process.

P13

Reduced growth hormone secretion in children and young adults following total body irradiation (TBI) for bone marrow transplantation (BMT) in childhood
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Introduction
Growth hormone deficiency (GHD) after cranial irradiation (CRI) is time, dose and fraction dependent. TBI (12–14.4Gy) involves low dose CRI, and skeletal

irradiation causing further adverse growth effects. We present baseline data from a prospective study of GH treatment.
Subjects $N=25$
We studied 13 BMT survivors (all had TBI, 3 also had CRI <18Gy), and 12 non-BMT subjects investigated for GHD. Both groups contained young GH-naïve children and young adults having end of GH-treatment retests and were well-matched for age, gender and pubertal status.
Methods
GH treatment was stopped >3 months before study if applicable.12 hr overnight GH profiles (GHP) were performed (20 min sampling 9pm–9am) and analysed by Cluster and Autodeconvolution software. Subjects slept at their usual time. 22 subjects also had an insulin tolerance test (ITT). Body composition was measured by DEXA.
Results
Median(range) age at and time since BMT were 5.8 (0.2–16.0) yrs and 3.5 (1.2–19.3) yrs respectively. Compared to controls, BMT survivors had increased % body fat (35.5(10.3) vs 25.5(12.8), $P<0.05$) and reduced peak GH levels in ITT (4.3(3.0) vs 7.7(5.0) μg/l, $P<0.05$) and their GHPs demonstrated reduced peak (3.5(1.5) vs 6.3(3.2) μg/l, $P<0.05$) and area under the curve (AUC) (7.0(3.4) vs 15.9(11.9) μg/l/min, $P<0.05$). Peak and AUC in GHP correlated with % body fat ($r=-0.45$, $P<0.05$ and $r=-0.55$, $P<0.005$). Covariate analysis showed that BMT had an additional effect on peak GH and AUC after adjusting for body fat, and that CRI had an additional effect to TBI. There was no gender effect. 7/8 adult BMT survivors were GH insufficient on retesting.
Discussion
These data indicate a significant reduction in GH secretion after BMT partly explained by increased adiposity. Additional TBI effects relate to hypothalamic-pituitary exposure and potentially altered feedback following skeletal irradiation. GHD was more pronounced in adult TBI survivors.

P14

Growth restriction with insufficient growth hormone production in a child with variant Miller-Dieker syndrome
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Introduction
We describe a girl presenting with abnormal facial features, growth restriction with insufficient growth hormone production and learning difficulties. She has an unbalanced translocation between 17p13.3 and 10q26.13 causing a microdeletion at 17p13.3 and trisomy of 10q26.
Case report
At presentation at 7½ years of age, her height was 4 cm below the 0.4th centile with a growth velocity of 1.6 cm/year; weight was on 0.4th centile. Investigations showed a bone age two years behind her chronological age, a poor increase in growth hormone production in response to the glucagon stimulation test (peak value 10.1 mU/l) and also a low Insulin-like growth factor 1 IgF1. In the first year of treatment with growth hormone she grew 8 cm. Thereafter, her rate of growth steadied at 4 cm/year.
Chromosome 17p13.3 deletions are most commonly seen in Miller-Dieker syndrome associated with lissencephaly. This patient has facial features in keeping with Miller-Dieker syndrome but no lissencephaly. This may be because the 17p13.3 breakpoint is unusually telomeric sparing the *LIS1* gene thought to be important in neuronal migration.
Conclusion
Growth restriction has been described in Miller-Dieker syndrome although there are no case reports describing growth hormone levels or supplementation in these patients. The presence of growth restriction with a proven reduction in growth hormone production in this case raises the question of whether there may be unidentified growth hormone deficiency in other patients with Miller Dieker syndrome and/or 10q trisomy. Further research in this area has the potential to contribute towards future management of these patients.

P15

Growth hormone therapy in the treatment of short stature in cardio-facio-cutaneous syndrome
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Background
The term "neuro-cardio-facial-cutaneous (NCFC) syndrome" describes a group of phenotypically overlapping syndromes that result from germline mutations in genes of the RAS-MAPKinase pathway. This pathway plays a role in growth factor signalling and short stature is a consistent feature of NCFC syndromes. This diagnostic group includes Noonan syndrome (NS) and cardio-facio-cutaneous (CFC) syndrome. Growth hormone (GH) has been used with good effect in NS. To our knowledge the effect of GH in CFC has yet to be reported.
Case Report
A female infant was born at term, birth weight SDS -0.34, following a pregnancy complicated by polyhydramnios. She was dysmorphic (posteriorly rotated low set ears, high forehead, depressed nasal bridge, antimongoloid slant of palpebral fissures). Cardiac assessment identified pulmonary artery branch stenosis and minor atrioseptal defect. A clinical diagnosis of NS was made. At 9.9yrs of age her height SDS was -3.15, bone age 9.2yrs, serum IGF1 12 nmol/l (normal range (NR) 15–101) and peak GH response to glucagon was 10.4 mU/l. At this time the phenotype was more consistent with CFC than NS. The diagnosis was confirmed by the identification of a BRAF gene mutation (c.770A$>$G). Treatment with GH (0.025 mg/kg/day) was introduced. After 4 months serum IGF1 was 34.2 nmol/l and IGFBP$-$35.8 mg/l (NR 0.8–3.4). GH dose was increased after 4 months to 0.035 mg/kg/day and after 8 months to 0.045 mg/kg/day. There has been no change in cardiac appearance or function and no reported adverse effects of GH therapy. 13 months after starting GH the patient has gained 0.6SD in height.
Conclusion
The growth response to GH treatment observed in this patient is similar to that reported in children with NS and less than might be expected given the biochemical features of GH deficiency. The efficacy of GH in this syndrome will only be elucidated in collaborative studies of patients with CFC.

P16

Two novel missense mutations in MRAP (p.Y59D and p.V26A) that lead to late onset Familial Glucocorticoid Deficiency (FGD) type 2
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Background
FGD is an autosomal recessive disorder causing glucocorticoid deficiency. Mutations in the ACTH receptor (MC2R) or the MC2R accessory protein (MRAP) cause FGD types 1 & 2 respectively. All the reported MRAP mutations result in abolition of a functional protein. This is reflected clinically as type 2 patients present early, no patient described to date has presented later than 1.6yrs. In contrast FGD type 1 mutations are usually missense and patients have a median age of onset of 2yrs.
Aim
To investigate the cause of disease in two families with late onset FGD. In family 1 the proband was diagnosed aged 5yrs. Family review revealed 2 older siblings with undiagnosed FGD. 1 sibling is well; the second has cerebral palsy secondary to a hypoglycaemic seizure. In family 2 the proband was diagnosed aged 18yrs with symptoms of fatigue, weight loss and depression.
Methods and Results
Coding exons of MC2R and MRAP were sequenced. ACTH dose response curves were generated for MC2R when transfected with wildtype (WT) or mutant MRAP constructs. MC2R trafficking with mutant Y59D MRAP was investigated using an immunofluorescence assay. MRAP gene analysis identified 2 novel homozygous missense mutations, c.175T$>$G (p.Y59D) in family 1 and c.76T$>$C (p.V26A) in family 2. Both mutants caused a right shift in the dose response curve and showed reduced cAMP generation in comparison to WT, this reached significance for the Y59D mutant. Immunofluorescence studies showed normal trafficking of MC2R to the cell surface when transfected with Y59D mutant MRAP indicating the defect is in signalling rather than trafficking.
Conclusion
These results describing late onset milder disease resulting from missense MRAP mutations indicate that disease severity in FGD patients reflects the functional significance of the underlying mutations.

P17

Severe glucorticoid deficiency in 17-hydroxylase deficiency – novel mutation in the CYP17A1 gene
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CYP17A1 is a key enzyme of human steroidogenesis, which is unique in that it catalyses two reactions, 17-hydroxylase activity and 17,20 lyase activity.

17-hydroxylase deficiency, a variant of congenital adrenal hyperplasia, results in hypertension and mild glucocorticoid deficiency. Loss of 17,20 lyase activity results in sex steroid deficiency, presenting with undervirilisation in boys (46, XY DSD) and lack of pubertal development in girls. Here we present the cases of two sisters with 17-hydroxylase deficiency presenting with severe glucocorticoid deficiency.

Case 1

A 4-week-old infant (46, XX) was assessed for prolonged jaundice and failure to thrive. A random serum cortisol was $<$ 25 nmol/l. A Synacthen test (with peak cortisol $<$25 nmol/l), normal 17-OHP and raised ACTH confirmed severe primary adrenal insufficiency. Gas chromatography/mass spectrometry (GC/MS) analysis of the urinary steroid pattern revealed predominant excretion of pregnenolone metabolites suggestive of combined and complete absence of CYP17A1 activities. Genetic test confirmed novel homozygous mutation of the *CYP17A1* gene yielding an early truncation of the CYP17A1 protein.

Case 2

A 6-week-old infant (46XX) and younger sibling of case 1 also presented with failure to thrive. Investigations confirmed primary adrenal insufficiency and genetic tests confirmed identical mutation as that of case 1. Their mother was identified to be a heterozygous carrier of the mutation.

Both girls are currently on Hydrocortisone supplements and doing well.

Conclusion

In 17-hydroxylase deficiency, relative increase of corticosterone with its glucocorticoid effect compensates for the lack of cortisol and hence rarely manifests with overt glucocorticoid deficiency. However in these two cases, very early truncation of the CYP17A1 protein explains the near total loss of activity with residual corticosterone secretion not sufficient to compensate for the loss of glucocorticoid synthesis in the early neonatal period. These cases further highlight the value of urinary steroid secretion analysis by the GC/MS in the differential diagnosis of adrenal insufficiency.

P18

Current use of the Synacthen Test: A questionnaire survey of British Paediatric Endocrinologists

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Background

Over the last two decades, supported by two metanalyses, the low-dose Synacthen Test (LDST) has gained in popularity, with many believing it to be more sensitive than the supra-physiological Standard (250 microgram) Short Synacthen Test (SSST). The literature reveals lack of consensus about its specific clinical applications, what is considered "low-dose" and how that dose is made up.

Methods

To ascertain current UK practice**,** we emailed a questionnaire to all UK based BSPED members ($N=257$), asking for a response from one representative from each department ($N=92$). This was followed up, one month later, by a further request to members of departments who had not returned the questionnaire.

Results

We received 39 replies, a departmental response rate of 42.4%. Most departments (29/39, 74%) still use the 250mcg SSST and 90% (35/39) employ some form of LDST. The 1 microgram dose was used by 44% of hospitals with the other 46% using 8 different doses based on age, weight and body surface area. The dose of the SSST also varied in 18% (7/39) The indications for doing a LDST or SSST varied, as did the method of making up the low dose with 14 different ways described by 23 hospitals. The most popular method ($N=5$) involved mixing 0.1 ml of synacthen (25 μg) with 50 ml of normal saline, to give a concentration of 500 ng/ml and administering a dose of 1 ml/m2. Additionally we found variation in the timings of cortisol sampling and the diagnostic cut offs for adrenal insufficiency. Increased requests for synacthen tests in asthmatic children were noted by 44% respondents since the 2006 recommendations with 67% reporting detection of adrenal suppression in10–50% of this group.

Conclusion

There is considerable variation in the methodology and application of the Synacthen test in assessing adrenal function. Is it time for standardisation?

P19

Congenital adrenal hyperplasia: incidence, prevalence and rationale for inclusion on the newborn screening programme in the Republic of Ireland

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Introduction

Congenital Adrenal Hyperplasia (CAH) carries a high risk of morbidity and mortality in undetected affected infants and has an estimated incidence of 1:15 000 based on newborn screening programmes internationally. This project aimed to identify cases and mode of diagnosis of CAH in the Republic of Ireland (ROI) to establish the case if any for screening.

Methods

(i) A retrospective questionnaire was sent to all consultant paediatricians in ROI confirming the number of cases of CAH attending their service and a follow up audit detailed presentation and diagnosis of cases from January 2000.

(ii) A prospective two year audit carried was carried out in conjunction with the Irish Paediatric Surveillance unit (IPSU) to ascertain the incidence of new cases from Jan 2007 to Dec 2008

Results

One hundred and nine consultants responded to the initial questionnaire declaring a total of sixty nine cases currently under their care in ROI. Of these, thirty one cases were diagnosed since January 2000. Only two cases had a positive family history of CAH. Eighty per cent of males presented less than one year of age (10–335 days) with features of salt wasting adrenal crisis. Two thirds of females presented with clitoromegaly or precocious adrenarche after the neonatal period while only one third of females were identified due to recognition of ambiguous genitalia at birth. Inclusion of 17 OHP on the neonatal screening card would have identified three of every four cases.

Prospectively only three cases were identified using IPSU correspondence.

Conclusion

The incidence of CAH in ROI is 1 per 13,621 live births. There is a strong case for the introduction of newborn screening for CAH in the Republic of Ireland due to the medical, psychological and economic benefits of early diagnosis prior to salt wasting crisis.

P20

Synacthen tests in children with asthma on high dose inhaled corticosteroids

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Background

Adrenal suppression is a well recognised complication of inhaled corticosteroids. Committee for Safety of Medicines (CSM) guidelines (2006) recommend that children taking high dose inhaled corticosteroids (HDICS) are tested for adrenal insufficiency. Patients requiring steroid replacement require a steroid card and written advice on steroid replacement in acute illness.

Aims

To determine the impact of CSM guidelines on the use of short synacthen test (SST) in asthmatics on HDICS 2) To evaluate the incidence of adrenal suppression in children on HDICS 3) To identify impending adrenal suppression in asthmatics on HDICS by comparing trends in basal plasma cortisol, peak plasma cortisol and plasma ACTH levels with those in non-asthmatics with a normal SST and no underlying pathology (control group).

Methods

Retrospective review of 85 case notes (38 pre- and 47 post-recommendations).

Results

There were 14 requests for SST's in children on HDICS in 2007–08 compared to 1 SST in 2004–05. Using the criteria of a peak cortisol of $<$500 nmol/l or an incremental cortisol rise of $<$200 nmol/l, 5/14 (35%) of the SST's were abnormal. 4 out of 5 asthmatics with abnormal synacthen tests received higher than recommended doses of inhaled steroids. There was no significant difference in the basal, peak cortisol levels and ACTH levels in the control group compared to asthmatics with a normal SST. All children on HDICS with adrenal insufficiency received corticosteroid replacement but there was no documentation of steroid card provision or written advice.

Conclusion

Current guidelines have resulted in increased monitoring of asthmatics on steroids. The incidence of adrenal suppression in our local population is similar to the studies done previously. We were unable to identify impending adrenal insufficiency in asthmatics with normal SST's. Clear documentation of patient care still needs to be addressed.

P21

Adrenal hypoplasia congenita presenting as sudden death in the newborn: how should we manage subsequent siblings?

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Introduction
Adrenal hypoplasia congenita (AHC) is often difficult to differentiate from congenital adrenal hyperplasia in the early stages of life. Both can present with severe salt-losing crises, and in some cases, even sudden, unexpected death. In particular there tend to be no abnormalities of the genitilia in AHC thus delaying a possible diagnosis. In the autosomal recessive form of AHC, the absence of a recognised single gene mutation can cause significant difficulties in genetic counselling and in the immediate and longterm management of subsequent siblings.
Case Series
We present three cases where the index child died suddenly, despite resuscitation, at 62, 12 and 19 h of age respectively. The diagnosis of AHC was made on post-mortem examination, based on adrenal size and histopathological appearance. From our experiences, we discuss potential difficulties that may be encountered, and we propose a management plan for dealing with future siblings. This plan includes admitting subsequent siblings shortly after birth to the neonatal unit for monitoring and evaluation of adrenal function.
Conclusions
Children with AHC can die suddenly and unexpectedly soon after birth. It is important that we devise a plan for further siblings of all children with AHC to ensure early detection and treatment.

P22

Nepalese StAR

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Introduction and Case report
Congenital adrenal hyperplasia (CAH) is a heterogenous group of conditions resulting from inborn errors of steroidogenesis, of which over 95% are due to 21-hydroxylase deficiency.
We present a 15-year-old Nepalese female, who was referred to the endocrine clinic for management of CAH. This diagnosis had been at 11 months of age, whilst resident in Hong Kong, when she presented acutely with vomiting and seizures. She had since been treated with fludrocortisone and hydrocortisone. Despite admitting variable compliance with hydrocortisone, she reported menarche at 12 years and regular menstruation. She had no evidence of virilisation or clitoromegaly, and had not had surgery. These findings were not suggestive of classical 21-hydroxylase deficiency. Karyotype was 46,XX. A urinary steroid profile confirmed complete adrenal insufficiency, and magnetic resonance imaging showed normal-sized adrenal glands. DNA analysis revealed a novel homozygous point mutation (G221D) in the steroidogenic acute regulatory protein gene (StAR), suggesting a diagnosis of lipoid CAH (LCAH). The glycine at codon 221 contributes to a hydrophobic cholesterol-interaction domain, which is likely disrupted by replacement with an acidic glutamate.
Discussions and Conclusions
The clinical importance of this case is two-fold. Firstly, the importance of re-evaluating a diagnosis when presented with unusual features is highlighted. StAR controls transfer of cholesterol across the mitochondrial membrane, and impairment results in severely compromised adrenal and testicular steroidogenesis. However StAR-independent ovarian steroidogenesis can result in spontaneous puberty in affected 46,XX subjects. Premature ovarian failure and anovulatory cycles due to ovarian cholesterol deposition are well recognised, however successful pregnancy with fertility support has been recently reported. This emphasises the importance of establishing this diagnosis to allow appropriate fertility counselling.
Secondly, the G221D mutation of StAR has not previously been reported. Functional studies are underway, which could provide additional insight into the molecular mechanisms of LCAH.

P23

The Androgen Status Of Young Women With Premature Ovarian Failure Depends On The Female Sex Steroid Replacement Regimen

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Aims
To compare the effect of a standard Sex Steroid Regimen (sSSR) with a physiological SSR (pSSR) on androgen status in young women with premature ovarian failure (POF).
Patient Population: Seven women with POF were evaluated for the study. The median age was 28 years (range 21–36) and the median duration of ovarian failure was 14 years (range 4–25).
Methods
An open label randomised, controlled, crossover study over 28 months comparing the effect of sSSR and pSSR on androgen status. Treatment consisted of a 12 month period of 4-week cycles of pSSR (transdermal estradiol 100 mcg daily for week 1 and 150 mcg for weeks 2–4 and either 200 mg progesterone vaginal pessaries or progesterone 10 mg orally twice daily in weeks 3-4), or sSSR (Loestrin 30, Galen Ltd; ethinylestradiol 30 mcg and norethisterone 1.5 mg daily for weeks 1-3, followed by 7 pill-free days), separated by run-in and wash-out periods. Serum Testosterone (T), Androstenedione (A4), SHBG were measured and the Free Androgen Index (FAI = {serum T/SHBG} $\times$ 100) calculated at months 0/6/12.
Results
At baseline in the sSSR group, median T, A4 and SHBG were not significantly different from those in the pSSR group. Median T at 6 and 12 months were 1.1 and 1 nmol/l (sSSR) and 1.6 and 1.8 nmol/l (pSSR). Median A4 at 6 and 12 months were 5.6 and 4.7 nmol/l (sSSR) and 5.5 and 6.4 nmol/l (pSSR). Median SHBG at 6 and 12 months were 105 and 110 nmol/l (sSSR) and 62 and 66 nmol/l (pSSR). Median SHBG was significantly higher in the sSSR group at 6 and 12 months ($P < 0.02$). Median FAI fell in the sSSR group from 2.4(2.2;7.4) at 0 months to 0.7(0.5;3.1) at 12 months ($P = 0.02$); this fall was not seen in the pSSR arm.
Conclusion
pSSR, not associated with any further decline in free androgen levels, is an attractive treatment for long-term replacement in young women with POF.

P24

Age at menarche and pubertal education in the London Borough of Islington

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There is data suggesting that puberty is starting earlier than in previous generations. However, there is minimal information on menarche and its management in UK primary schools. We present a population study, performed in Islington: a London borough with wide ethnic diversity, conducted using written questionnaires to all primary schools. Data collected included: information on menarche, provision and disposal of sanitary towels and teaching on puberty. 22 (50%) replies were received, incorporating data on 867 year 5&6 girls (435 year 6 girls; 432 year 5 girls).
In year 6, 17% of girls had achieved menarche [35% Black (Black Caribbean, Black Other, Somali, Other Black African ethnicity codes); 20% British White; 14% Mixed; 12% Turkish; 8% other white; 5% Bangladeshi; 4% other Asian; 2% unknown]. In year 5, 3% had started menstruation [33% Mixed; 17% Black; 17% British White; 17% Turkish; 8% Bangladeshi; 8% unknown].
Girls had access to sanitary towels in 91% of schools, (with some overlap: 55% from the school office; 36% from teachers; 18% from the sickroom). Most schools (95%) provided sanitary bins but only one had bins in all toilets. Cost was not a factor in the provision of sanitary facilities in 77% of schools.
Ninety one % of schools included teaching on puberty and periods in year 6; 76% in year 5; 41% had no designated teaching in earlier years.
This study demonstrates the large proportion of menarchal girls in London primary schools (over a third of Black ethnicity). Almost all schools provided sanitary bins. Pubertal education occurred in most but not all schools.
Menarche, a late sign of pubertal development, is achieved by 1 in 6 girls in their final year of primary school in Islington. Provision in schools needs to reflect this and education on puberty should start earlier and take place in all primary schools.

P25

Diagnostic Challenges in Androgen Insensitivity Syndrome & 5 Alpha Reductase Deficiency

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Introduction
The clinical differentiation between androgen insensitivity syndrome (AIS) and 5 alpha reductase deficiency (5-ARD) can be difficult. Presenting features may be similar and initial investigations may still not be discriminatory.
Methods
Case notes on a total of ten patients with the initial diagnosis of AIS or 5-ARD were retrospectively reviewed.
Results
All ten children had a 46XY male karyotype. Four children were raised as male. Three out of the six females had an initial diagnosis of AIS, but subsequent re-evaluation revealed a diagnosis of 5-ARD. The age at diagnosis in the 5-ARD group ranged from birth to 12.4 years. A sibling pair who had had previous gonadectomies and negative androgen mutations on genetic analysis was reinvestigated due to the development of clitoromegaly. A urine steroid profile (USP) and then genetic analysis confirmed the diagnosis of 5-ARD. A child whose sibling had complete AIS also subsequently had a diagnosis of 5-ARD on urine steroid profile. Interestingly, one male infant presenting with micropenis had post HCG testosterone: DHT ratio of 7. A diagnosis of 5-ARD was subsequently made on urinary steroid profile and confirmed on genetic testing.
Conclusion
This series revealed that clitoromegaly and inguinal lumps were a common finding in females with 5-ARD. Thus females with a diagnosis of AIS were re-evaluated and subsequently 3 of them were reclassified as 5-ARD. Furthermore the post HCG testosterone: DHT ratio may not be diagnostic of 5-ARD. We reinforce the need to evaluate these children using a combination of USP, HCG test & genetics.

P26

Prevalence of congenital malformation in Scottish children with true congenital hypothyroidism 1979–2009

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Introduction
The prevalence of congenital malformations (CM) in congenital hypothyroidism (CH) is higher than expected, particularly for cardiac malformations, but the published data vary considerably – from 2.4% to 24% – in different series.
Methods
Using existing databases for CH and Scottish population statistics, we have retrospectively determined the prevalence of cardiac, non–cardiac and syndromic disorders in Scotland since the introduction of newborn screening.
Results
Five–hundred and six cases of true CH have been logged in Scotland since 1979 including 489 born between 1980 and 2008, giving a period prevalence of 1:3,617 live births. Twenty–five children had the following disorders: *Dysmorphic* syndromes (9) – pseudohypoparathyroidism (PHP)1a (1), PHP1b (1), Pendred syndrome (2), Sotos (1), Beckwith–Wiedemann (1), 14;15 translocation (1), unclassified (2 – one died); *cardiac* (7) – PDA (2 –1 preterm, 1 died), VSD (2), Truncus arteriosus (1 –died), Pulmonary stenosis (PS) (1), ASD, PS and anomalous pulmonary veins (1); *non–cardiac*: developmental dysplasia of hip (DDH) (4, 1 with cleft palate), oral cleft (2, 1 with dysmorphic features, 1 with DDH), hypoplastic right kidney (1), deafness not associated with Pendred syndrome (2), extra digits (2 siblings), myelomeningocele with hydrocephalus and talipes (1). Twelve children had multiple malformations. Excluding the 4 children with PHP & Pendred syndrome, the prevalence of congenital and cardiac malformation in the cohort of 506 children was 4.2% and 1.4% compared with 3.2% and 0.5% respectively for the Glasgow Registry 1980–97.
Conclusion
The overall prevalence of congenital malformation in Scottish children with true CH is only slightly higher than that of the general Scottish population and less than reported elsewhere. This difference may reflect smaller cohorts and the inclusion of newborns with transient hyperthyrotropinaemia in other series.

P27

Factors that influence the decision to perform a karyotype in suspected disorders of sex development: lessons from the Scottish Genital Anomaly Network Register

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Background
The Scottish Genital Anomaly Network(SGAN) is a national managed clinical network that provides care to patients with a suspected disorder of sex development(DSD). Factors that influence the decision to perform a karyotype in suspected DSD are unclear.
Aim
To explore the SGAN register to study the factors that influence the decision to perform a karyotype. Variables examined included centre of presentation, examination findings and associated malformations. An external masculinisation score(EMS) was calculated in cases with detailed records of genital examination.
Results
Out of the 498 cases on the register, 306(61%) were diagnosed as having non-specific disorder of undermasculinisation(NSDUM) and in 119(24%) the diagnosis was unclear; 396(80%) cases were assigned male sex; 79(16%) were assigned female and in 23(4%) cases data were unavailable regarding sex of rearing. Karyotype was reported to be performed in 71/498(14%) cases overall and in 33/306(11%) cases of NSDUM. Out of 125 cases where an EMS could be calculated, the median EMS(5^{th},95^{th}) of cases who had a karyotype and who did not have a karyotype was 6.5(0,11) and 11(5,11), respectively ($P < 0.0001$). Associated malformations were recorded to be present in 35/498(7%) cases, and 19(54%) of these cases had a karyotype performed. Comparing the two centres with the highest number of cases in the register, report of a karyotype was present in the register for 6/90(7%) cases from Aberdeen and 65/342(19%) cases from Glasgow. The median EMS scores of these cases in Aberdeen and Glasgow were 8.5 (1,11) and 7.5 (0,11), respectively.
Summary
These data represent the first attempt at benchmarking the decision to check a karyotype in infants with suspected DSD. Whilst this decision may be related to the complexity of the genital anomaly, there are other factors that may influence this, and these require further exploration through more rigorous systems for data collection.

P28

46 XY girls – the importance of careful newborn examination

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Introduction
Disorders of sexual differentiation (DSD) are uncommon and pose many challenges to families affected and clinicians. The genotypic 46XY male with female phenotype form an interesting group with diverse presentation. We studied all such children attending our multidisciplinary DSD clinic. Only in a minority of these children did newborn examination raise the possibility of DSD. Delays in identifying these abnormalities can cause significant psychological difficulties in both child and their family. Healthcare professionals performing neonatal checks need to be vigilant in the examination of babies' genitalia so that specialist input and assignment of sex can be performed promptly.
Materials and Methods
Case-notes drawn from a prospectively maintained database were reviewed and data gathered on age at presentation, family history, findings on genital examination, underlying diagnosis.
Results
Eleven children were studied, all raised as girls. Median age at presentation was 18 months [range 0 days - 15 years]. At presentation, 6/11 had palpable gonads, 4 of whom also had single perineal opening (urogenital sinus, UGS). 6 children had an enlarged phallus.
In only 3/11 girls the possibility of DSD was raised during newborn examination. In the remainder, 2 children each were picked up by karyotype (incidental finding), palpable gonads, sibling screening, and 1 each of UGS, and delayed puberty. 5/11 of our study group had a sibling with DSD. The ultimate diagnosis is unknown in 8 (normal androgen binding in 7, results pending in 1), and 1 each have mixed gonadal dysgenesis, 5 -alpha reductase deficiency, complete androgen insensitivity, complete sex reversal.

Conclusion
In our diverse group of 46XY girls, only a small minority were picked up during the neonatal period. Many girls at presentation had clinical signs including palpable gonads, UGS or enlarged phallus. This emphasizes the importance of thorough neonatal genital examination for early diagnosis of DSD, especially in those with positive family history.

P29

46, XY DSD: A case of clinical and biochemical conflict

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Introduction
We describe a case of 17- beta hydroxysteroid dehyrogenase Type III (17-βHSD3) deficiency in a girl from the travelling community. This case demonstrates how the clinical picture may not correlate with the biochemical results.
Case
A 4.7 year old girl presented for elective hernia repair. Intraoperatively, what was felt to be a testis was palpated. Investigations revealed a 46, XY karyotype. Pelvic ultrasound demonstrated absence of mullerian structures. Bilateral palpable gonads in the inguinal region with normal female external genitalia were found on clinical examination.
Family history was very difficult to obtain as parents were reluctant for disclosure of information. However, it was revealed that two maternal first cousins had presented with delayed puberty and required bilateral gonadectomies.
Initial impression was that of complete androgen insensitivity syndrome (CAIS) or a defect in testosterone biosynthesis. However, testosterone was undetectable with only a small increment in androstenedione post HCG stimulation. Androgen receptor (AR) sequencing revealed no mutations in the AR gene thus eliminating CAIS. Serum inhibin and anti-mullerian hormone (AMH) were detectable at 63 ng/l and 222 pmol/l respectively indicating the presence of functioning testicular tissue. A 24 h urine steroid profile was reported as normal with no evidence of an androgen biosynthesis defect. Further ongoing DNA analysis revealed no mutations in the SF1 or SRY genes but a positive mutation in intron 3 of the 17-βHSD3 gene.
Conclusion
Open communication is necessary for optimal investigation and management in 46, XY DSD individuals. However, confidentiality must be paramount. Ongoing research into molecular studies will allow for more precise diagnosis in these patients in the future. However, genetic testing is guided by the clinical and biochemical information. This case highlights the importance of continuously recalling the clinical picture despite conflicting biochemical results.

P30

Congenital hypothyroidism – A thirty year audit of the National Newborn Screening Programme in the Republic of Ireland

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Introduction
Congenital hypothyroidism (CHT) has a reported incidence of 1:3500 in Caucasian populations. Early detection by newborn screening and appropriate L-thyroxine treatment leads to normal or near-normal neurocognitive outcome.
The National Newborn screening programme (NNP) was established in Children's University Hospital, Temple St. in 1979. This study aimed to ascertain the incidence of congenital hypothyroidism in the Republic of Ireland (ROI) and to evaluate the screening programme with regard to time taken to diagnosis, initiation of treatment and the contribution of scanning to diagnosis.
Methods
An audit was performed of all positive screens for CHT between July 1979 and December 2008. Date of detection, clinical presentation, thyroid function tests and technetium scan results (from 1990) were reviewed.
Results
A total of 648 children have been diagnosed with CHT. The incidence of CHT was 1 case per 2296 live births in the Republic of Ireland (ROI) in the past decade with increasing numbers over recent years. Sixty five percent of cases were female (male $=221$, female $=403$, unreported $=24$). A median of 22 cases were reported annually (range 14–44). The median time to sample collection was 5 days and median time to detection of an abnormal sample was 9 days. Scan information was available on 368/459 cases screened since 1990 discriminating between thyroid agenesis ($n=87$), ectopic/small thyroid ($n=164$), dyshormonogenesis ($n=58$), and normally placed thyroids ($n=59$). Mean TSH on screening card compared to scan results were 230 mU/l (agenesis), 162 mU/l (ectopic thyroid), 60mU/l (dyshormonogenesis) and 78 mU/l (normal thyroid).
Conclusions
The CHT screening programme has been successful in the early detection of affected cases. A target time of 10 days is been evaluated. Reasons for the increase in incidence of CHT in recent years require further investigation.

P31

Prophylactic Thyroidectomy in Children with Multiple Endocrine Neoplasia Type 2

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Background
The most common cause of death in patients with Multiple Endocrine Neoplasia type 2 is medullary thyroid carcinoma. All patients with MEN2 develop this cancer and Prophylactic Thyroidectomy (PT) is recommended to prevent malignant transformation.
Method
This study reviews our experience of treating children identified as carriers of a RET mutation diagnostic of MEN-2A. Data was collected by reviewing patient notes and hospital electronic databases.
Results
Between 1998 and 2009 15 children (8 boys; 7 girls) were identified by genetic analysis as having MEN 2. The commonest codon with RET mutation was 634Y ($n=8$), 2 siblings were positive for 891A, 2 further siblings were 790F positive and 1 child had codon 620G mutation. Of these, 13 underwent PT and 3 central lymphadenectomy (2 are awaiting surgery). Median patient age of those undergoing surgery was 7.5 years (range 3.5–15 years) and median hospital stay was 4 days. 10 children had transient hypocalcaemia following surgery and required oral calcium ($n=10$) and alfacalcidol ($n=3$). There were no other post-op complications. Histology showed medullary carcinoma in 4 specimens (completely excised) C-cell hyperplasia in 8 cases, and 1 case showed non-specific thyroiditis only. There were no lymph node metastasis and all children but one have undetectable calcitonin levels.
Discussion
This is the first UK case series of children with MEN2 undergoing prophylactic thyroidectomy. We have shown PT to be a rare but safe procedure. We propose to conduct a UK audit of prophylactic thyroidectomy in children with MEN2.

P32

Has the change in Guthrie TSH cut off point made an impact in early detection & management of congenital hypothyroidism?

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Introduction
Neonatal thyroid screening commenced in the UK in 1981. The TSH cut off point cut off point has changed from 80 mu/l to 25 mu/l over the period for early detection and referral. From April 2006 in the West midland this has dropped to 20 mu/l as upper level and 10 mu/l as lower level.
Method
Retrospective audit was undertaken in our hospital on babies referred with an abnormal Guthrie test for a period of 13 years from April 1996 to April 2009. Results were compared between 1996–2006 and 2006–2009 to see the impact on the change in Guthrie TSH levels.
Results
There were 20 cases referred in 10-year period during 1996–2006, and 18 cases in 3-year period, during 2006–2009. Lowering upper cut off point from 25 to 20 μ/l picked up 4 additional cases.

Four cases were picked up by lower cut off point (> 10 μ/l), could have been picked up by the previous lower cut off point (> 13 μ/l) as all the values were above 13 μ/l. 3/18 cases (17%) have not required treatment but needed regular monitoring and follow-up.
Conclusion
Number of referrals has increased from 2 cases per year during 1996–2006 to 6 cases per year during 2006–2009.
4/18 cases (22%) were picked up by lowering high cut off point, but lowering the lower cut off point has not picked up any additional cases.
There has been an increase in patient referrals and clinical workload following the change in recent TSH guidance.

P33

Is There A High Incidence Of Graves' Disease In Doncaster And What Are The Potential Causes? A Retrospective Study

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Graves' disease is the most common cause of hyperthyroidism in children. The incidence in the UK and Ireland is unknown but estimated to be 0.84 per 100 000 people (0–15 yr olds). Due to an apparent high local incidence, a retrospective study was conducted on patients diagnosed with Graves' disease in a district general hospital in the locality.
Aim
To evaluate the clinical features, investigations and treatment of patients diagnosed from 2004 onwards and to identify possible causes.
Method
A proforma was designed prior to data collection. Case notes and investigation reports were reviewed.
Results
Seven patients were identified (6 females, 1 male) with a mean age at diagnosis of 13.9 years (range 12–15 years). This gives a local incidence of 2.43 per 100 000 people (0–15 yr olds). The most frequent symptoms were heat intolerance (71%), anxiety (57%), irritability (57%), palpitations (57%) and weight loss (57%). The most frequent signs were goitre (86%) and tremor (57%). Thyroid peroxidise autoantibodies were found in all 7 cases and thyroid-stimulating hormone receptor antibodies were found in 86% of cases. All 7 patients received block and replacement therapy and 3 patients required propanolol for palpitations. Three patients achieved remission with a mean duration of treatment of 47.5 months. One patient had a total thyroidectomy.
Conclusion
Whilst considering the small sample size, the local incidence of Graves' disease could be higher than the incidence for the UK and Ireland. Studies on monozygotic twins have demonstrated an environmental influence to the multifactorial aetiology with the susceptibility to the development of Graves' disease due to non-genetic factors estimated to be 21%. Smoking is one factor that has been related to Graves' disease and in our region there is a greater prevalence of smokers than the UK as a whole. Other potential factors include infection and high iodine intake.

P34

What skills do young people attending paediatric endocrine clinics feel they need before transfer to adult services?

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Background
A key element of the transition process is encouraging young people (YP) to become more independent in their healthcare. However it is not known what skills YP feel they need before being ready for transfer to adult services.
Method
A simple questionnaire was designed for YP to rate out of 5 A. their current status in terms of 5 aspects of independence in healthcare (5 "yes, I do it all of the time" to 1 "no, my family does it for me"); B. how important they are at the time of transfer (5 "totally important", 1 "not at all important") and C. their preparedness for transfer (5 "totally prepared" and 1 "not at all prepared"). A signed rank test was performed between their current status and their ideal status at transfer and regression analysis was performed to identify which aspects were associated with feeling more prepared.
Results
The questionnaire was administered to 72 YP (37 male) with long term endocrine conditions. The mean age was 15.5(2.5) years old. 31% of YP were aware that transition or transfer had been discussed, however only 11% were aware of what the plan was. The following aspects of independence in healthcare were felt to be at least fairly important at the time of transfer (rate 3+) were:- organizing and taking medication in 79% of YP (75%); seeing the doctor alone in 72% (21%)*; asking questions in clinic, in 69% (63%); organizing and collecting prescriptions in 63% (29%)* and phoning endocrine service with questions in 43% (14%)* (*$P < 0.05$ significantly different from current status). Using stepwise regression the factors associated with feeling prepared for transfer were confidence to be seen alone and organizing and taking medication.
Conclusion
To prepare for adult services YP have identified a need to increase independence in healthcare. Doctors and nurses should do more to encourage this, particularly by giving YP the opportunity to be seen alone in clinic.

P35

Point of care glucose monitoring on the Neonatal Unit: An audit project

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Introduction
Assessment of hypoglycaemia in neonates is challenging due to limited blood availability, and lower glucose readings compared to adults. ISO criteria used to assess the accuracy of glucometers are based on adult needs where values below 4.2 mmol/l require intervention. National neonatal guidelines define an action threshold for hypoglycaemia as a glucose below 2mmol/l. We currently use a Radiometer ABL-735 blood gas analyser which uses 35 microlitres of blood. We trialled the Nova Statstrip glucometer (NSG), which uses 1.2microlitres of blood, and internally corrects for haematocrit.
Aims
To compare the accuracy of the NSG against the Radiometer and establish if the NSG could be a reliable alternative for gluco-analysis on the unit.
Method
We reviewed paired glucose readings from the NSG and Radiometer, collected prospectively between December 2008 and February 2009 from babies on the unit. We performed statistical tests to assess the accuracy and precision of the NSG compared to the Radiometer.
Results and Conclusion
We obtained 730 validated paired values. 166 had a value less than 4.2 mmol/l on the Radiometer, 10 below 2 mmol/l and 2 below 1 mmol/l. 98.80% of NSG values less than 4.2 mmol/l and 97.70% of values greater than 4.2 mmol/l met the ISO criteria. Bland-Altman and linear regression analysis showed good correlation between the readings (r-squared = 0.8259). An Error Grid showed that most infants would be appropriately managed as per our local guidelines when Radiometer values were below 2 mmol/l. The NSG performed well on statistical analysis compared to the Radiometer, and performed well across a wide range of haematocrits. We recommend its use on our unit.

P36

What do young people think about seeing the doctor alone in paediatric endocrine clinics?

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Background
Seeing the doctor alone has been associated with a better outcome following transition to adult services.
Methods
A simple questionnaire was designed for young people (YP) to enquire about being seen alone in paediatric endocrine clinics.
Results
The questionnaire was administered to 72 YP young people (37 male) with long term endocrine conditions. The mean age was 15.5 (2.5). 10% of YP thought they should be offered the opportunity to be seen on their own at any age, 7% from the age of 11, 19% from the age of 14, 25% from the age of 17, 22% thought it depended on maturity not age and 14% were unsure. Of those that stated an age 40% of all the YP were the age that they felt they should be offered an opportunity to be seen on their own. 32% of YP were either totally or very confident to be seen

alone, 21% were fairly confident and 24% were a little confident and 21% were not confident at all. However only 21% of YP reported ever having seen the clinic doctor alone and only 19% reported the doctor ever having suggested it. The most popular reasons stated by YP for wanting to be seen alone were "I get the opportunity to talk about things in private/confidence" in 35% of YP and "I get the opportunity to help the doctor make decisions that are right for me" in 31% of YP. The most popular reasons stated by YP that they currently haven't or wouldn't be seen alone were "I like having my parents there for company/support" in 58% of YP and "My parents like to hear what the doctor says" in 54% of YP.

Conclusion

At least 40% of YP feel that they are an appropriate age to be offered the opportunity to be seen alone in clinic with >50% feeling at least fairly confident to do so. However this questionnaire demonstrated that YP are not being given this opportunity.

P37

Pitfalls of the four hour wait: keeping alert to potential endocrine presentations in Accident and Emergency

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Background

Emergency staff are under pressure to assess and refer within tight targets. Two adolescents presented to A&E with psychiatric symptoms, were referred to Child and Adolescent Mental Health (CAMH), but fortunately came to our attention and were diagnosed with thyroid disorders.

Case 1

Fifteen-year-old boy presented with a two week history of disturbing auditory hallucinations and was referred to CAMH. He was commenced on antipsychotic medication. The A&E doctor did ask for a Paediatric opinion as he "was lacking facial hair". OE Ht < 0.4th C, Wt >25th C, facial features of myxoedema, smooth goitre, sparse dry hair and bilateral hydroceles. Investigations: TSH > 150 miu/l (0.25–5), FT4 4 pmol/l (9–23), TPO antibodies > 1000 iu/l. The antipsychotic medication was stopped, he was treated with thyroxine and his hallucinations resolved.

Case 2

Fourteen-year girl presented with "panic attacks", anxiety, auditory hallucinations and compulsive behaviour. CAMHs staff commenced Sertraline. At her routine asthma follow up HR was 120 bpm, proptosis, goitre and tremor. Investigations TSH < 0.1 miu/l, FT4 > 100. Within three months of carbimazole her psychiatric symptoms resolved.

Discussion

Although it is well recognized that adults presenting with acute psychotic symptoms may have thyroid disease, there does not appear to be the same recognition in children. Previous studies have indicated that the yield from "routine screening" TFTs in Paediatric Psychiatry patients is low and that no clear correlation appears to exist between psychiatric presentation and degree of severity in thyroid dysfunction. However, all health care professionals should be alert to patients who have additional symptoms and signs of thyroid disorders, particularly goitre. Appropriate treatment usually results in resolution of psychiatric symptomatology.

P38

Management of central diabetes insipidus in a paediatric intensive care unit

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Background

Central diabetes insipidus (CDI) is rare in infants and children. Up to 30 percent of cases are idiopathic and its clinical presentation is poorly defined. In critically ill paediatric intensive care unit (PICU) patient with CDI, there is increased risk of brain damage and death due to severe hyperosmolarity, hypovolaemic shock, hypernatraemic seizures or complications of treatment.

Aim

To assess the causes, management and outcome of CDI in patients admitted to a tertiary PICU with a large neurosurgery and oncology service.

Method

Retrospective data were collected in PICU patients who required assessment of serum and urine osmolalities over a period of 3 years (2006–8).

Results

A total of 58 patients**,** 7/58 (12%) had CDI, 1/58 (1.7%) had nephrogenic DI and 10/58 (17.2%) had incomplete DI or solute diuresis. Brain tumours were the commonest cause of CDI. All patients with CDI received full maintenance fluids of: 0.9% sodium chloride ($n=5$), 0.45% sodium chloride/5% dextrose ($n=1$), or oral feeds ($n=1$). Only 2 patients required replacement of fluid losses which were estimated as urine output plus 10% of body weight. An initial dose of intravenous DDAVP was required in 6 patients. One patient was treated with oral DDAVP and had developed SIADH during treatment. He had a hyponatraemic seizure and was treated with 3% sodium chloride infusion and 50% fluid restriction. All patients were monitored by hourly urine output and 4-hourly blood gases for electrolytes level. Repeated doses of DDAVP were required in 4 patients following breakthrough episodes. We discharged 3 patients home on regular DDAVP, transferred 1 to another hospital and 3 died because of their primary illness.

Conclusion

PICU patients with CDI need prompt fluid management, close monitoring of urine output and electrolytes as well as appropriate DDAVP doses to avoid serious complications of the disorder and management pitfalls.

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