Poster Presentations

Poster No. 001

Withdrawn.

Poster No. 002

Quality improvement project on the investigation, assessment and management of childhood epilepsy

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Objective: Epilepsy affects one in every 200 children and young people in the UK. The Epilepsy12 National report published by RCPCH in 2014 recommended hospitals to review services for improvement with a focus on appropriate diagnosis, investigation and management. Consequently, the aim of this project was to 1. Investigate the assessment and management of epileptic patients in a large hospital trust 2. Explore patient demographics 3. Compare local trust data with national data.
Methods: Outpatient clinic and inpatient discharge letters were audited retrospectively for 40 patients who had been followed up for at least a year. Areas explored included: 1. Patient demographics 2. Diagnosis of epilepsy including professional input 3. Assessment, classification and management of epilepsy.
Results: Demographics: 23 (57.5%) were males and 17 (42.5%) were females. Age of diagnosis ranged from 2 months to 15 years. 15 (37.5%) had a psychiatric or cognitive comorbidity. Professionals: 13 patients (32.5%) had an input by a consultant paediatrician with a special interest in epilepsy and 4 (10%) were referred to an epilepsy specialist nurse by 1 year. 23 (57.5%) were referred to a tertiary centre. Assessment and classification: 28 (70%) had evidence of appropriate first clinical assessment. 40 (100%) of patients had an EEG. 30 (75%) had an MRI. 36 (90%) were classified by seizure type and 17 (42.5%) by epilepsy syndrome category. Management: 12 (30%) were treated with carbamazepine with 10/12 (83.3%) having no contraindications to be on carbamazepine. (12.5%) were given advice regarding physical activity or water safety. 36 (90%) still had their diagnosis at 1 year.
Conclusions: There was little evidence of dissemination of advice regarding physical activity and water safety. Access to epilepsy nurses and epilepsy specialists is essential for appropriate safety advice and management. Psychiatric and cognitive comorbidities highlight the need for effective mental health services.

Poster No. 003

What are the perspectives and understanding of healthcare professionals including occupational therapists on treatment and care of babies with infantile spasms and early-onset epilepsy? A qualitative design

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Objective: To explore the perspectives and understanding of Allied Healthcare Professionals (occupational therapists, physiotherapists, speech & language therapists) that work with children and epilepsy in order to guide and advocate for this population group.
Methods: A qualitative study design using interpretive thematic analysis with the data from participants in 10 semi-structured interviews.
Results: The professionals had worked across acute and community settings and had previous experiences of working with children with epilepsy with some awareness of these needs. There were 5 themes that emerged: (1) housing and social needs, (2) epilepsy, psycho-social and mental health needs, (3) therapy approaches, (4) training for allied healthcare professionals, and (5) adolescents, young girls, women and epilepsy.
Conclusions: There are gaps in service provision for certain areas and will be shared within the presentation. Epilepsy requires additional considerations for safety that other conditions may not require. It is crucial in the interests of public health for children and families with epilepsy to be able to advocate for resources and their specific needs.

Poster No. 004

Time to onset of cannabidiol (CBD) treatment effect and resolution of adverse events in patients with Dravet syndrome: pooled analysis of two randomised controlled trials

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Objective: To estimate the time to onset of treatment effect of add-on cannabidiol (CBD) in reducing convulsive seizure frequency associated with Dravet syndrome (DS) using a post-hoc pooled analysis of 2 phase 3, randomised, placebo-controlled trials (GWPCARE1/NCT02091375; GWPCARE2/NCT02224703).
Methods: Patients received GW Pharmaceuticals' plant-derived, highly purified CBD medicine (100mg/mL oral

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solution) at 10mg/kg/day (CBD10; GWPCARE2) or 20mg/kg/day (CBD20; both trials) or placebo for 14 weeks. CBD treatment started at 2.5mg/kg/day and reached 10mg/kg/day on day 7 and 20mg/kg/day on day 11. Percent reduction in cumulative convulsive seizure frequency for each treatment day (including previous treatment days) and timing of adverse events (AEs) were assessed.

Results: Overall, 194 patients were randomised to CBD and 124 to placebo. CBD led to significantly greater percent reductions in convulsive seizure frequency than placebo in GWPCARE1 (CBD20 39% vs placebo 13%, p=0.0123) and GWPCARE2 (CBD10 49%, CBD20 46% vs placebo 27%, p=0.0095 and p=0.0299). In the pooled data, treatment differences in seizure reduction emerged during titration and were maintained throughout the study, with nominal significance (p<0.05) achieved by day 13 for CBD10 and day 12 for CBD20. Onset of the first reported AE occurred during titration in 60% of patients with AEs. AEs resolved within 4 weeks of onset in 40% of patients and by the end of the study in 60%. Increases in ALT/AST (>3× upper limit of normal) occurred in 3 (5%) patients for CBD10, 25 (19%) for CBD20, and 1 (1%) for placebo; all were on concomitant valproate. All elevations resolved, either spontaneously while continuing CBD, after discontinuing CBD, or after reducing CBD, valproate, and/or clobazam dose.

Conclusions: CBD treatment effect (seizure reductions and AEs) may occur early, during titration. The majority of AEs resolved during the study.

Poster No. 005

Low dose fenfluramine hydrochloride oral solution provides long-term, clinically meaningful (≥50%) reduction in seizure frequency in Dravet syndrome: interim analysis of a long-term open-label extension study

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Objective: To characterize long-term safety and durability of effect for adjunctive fenfluramine (FFA) in treating Dravet syndrome (DS).

Methods: Patients (2–18y) with DS entered a long-term open-label extension (OLE) (1503) after completing one of two Phase 3 studies: Study 1 (14wks; placebo or FFA 0.2 or 0.8mg/kg/d [max, 30mg/d] or Study 1504 (15wks; placebo or FFA 0.5mg/kg/d [max, 20mg/d]). Stiripentol was excluded in Study 1 but mandatory in Study 1504. In 1503, patients received FFA 0.2mg/kg/d for month 1; dosing was titrated to effect thereafter. Effectiveness and tolerability were assessed at months 1, 2, and 3, then at 3-month intervals.

Results: At interim analysis (13-Mar-2018), 158/187 patients continued into OLE; 89% completed 12 months of FFA (mean dose, 15.2mg/d; median duration, 400d [range, 71–703d]). During the entire OLE, median percentage change in monthly convulsive seizure frequency (MCSF) for FFA vs pretreatment Phase 3 study baseline was –63.6% (p<0.001); clinically meaningful (≥50%) and profound (≥75%) MCSF reduction from baseline were 63% and 41%. At month 12, median and mean longest interval between convulsive seizures were 26 and 60 days (range, 2–589d); 71% of caregivers and 83% of investigators rated patients 'Much improved/Very much improved'. The most common adverse events included appetite decrease, pyrexia, nasopharyngitis, and diarrhea. No valvular heart disease or pulmonary hypertension was observed in any patient.

Conclusions: Treatment with FFA resulted in robust, sustained reductions in MCSF and was generally well tolerated. No valvular heart disease or pulmonary arterial hypertension was observed in any patient at any time. FFA may be an important, novel antiepileptic drug for long-term DS treatment.

Poster No. 006

ZX008 (low dose fenfluramine hydrochloride oral solution) provides long-term, clinically meaningful reduction of convulsive seizure frequency in young (<6 years old) Dravet syndrome participants: analysis from a long-term open-label study

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Objective: A recent study examining epilepsy onset before 2 years of age identified uncontrolled seizures as a predictor of poor developmental outcome. We conducted a post-hoc analysis of the efficacy and safety of ZX008 in patients with Dravet syndrome (DS) <6 years old.

Methods: Patients (2–18y) with DS entered an open-label extension (OLE) study after completing one of two phase 3 studies. In the OLE, all participants initially received 0.2mg/kg/day ZX008 for 1 month; dosing was then titrated to optimal effect (maximum dose 0.8mg/kg/day [maximum 30mg/day] or in patients also receiving stiripentol, 0.5mg/kg/day [maximum 20mg/day]).

Results: A total of 42 of 158 (26.6%) participants who enrolled in the OLE were <6 years old upon entry into the phase 3 studies. The median baseline monthly convulsive seizure frequency (MCSF) before double-blind treatment was 10.7 seizures/month (range, 4.0–147.3) in this patient subgroup (<6y). At the time of the OLE interim analysis, the median decrease in MCSF in the <6 years subgroup over the entire observation period compared to baseline was –75% (p<0.001) compared with –64% in the overall study population (2–18y). The most frequently reported adverse events included pyrexia, upper respiratory tract infections, decreased appetite, and diarrhea. No valvular heart disease or pulmonary arterial hypertension was observed.
Conclusions: Treatment with ZX008 provided sustained, clinically meaningful reduction in MCSF in DS participants <6 years old. Importantly, effective control of seizures in this young age group might be expected to mitigate the negative neurodevelopmental outcomes reported to be associated with treatment-refractory seizures.

Poster No. 007
The improving provision of epilepsy care for children in England and Wales

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Objective: Epilepsy12 is a UK collaborative clinical audit of health care for children and young people with suspected epileptic seizures managed by the Royal College of Paediatrics and Child Health (RCPCH). Round 3 began in April 2017 as part of the National Clinical Audit and Patient Outcomes Programme (NCAPOP). The audit consists of organisational and clinical domains and Patient Reported Experience Measures. We present results describing paediatric epilepsy services in April 2018.
Methods: All relevant Health Boards and Trusts (HB/T) were invited to register to participate and identify a HB/T lead. A snapshot survey was completed via a bespoke online platform by the HB/T lead describing local provision as of April 2018. Data was analysed by the RCPCH including regional and national aggregates and longitudinal comparison to previous 2012, 2014 reports.
Results: 148 HB/T with a paediatric epilepsy service across England and Wales registered to participate and submitted data. 94.6% (140/148) of HB/T employed a consultant paediatrician with expertise in epilepsy; 77.7% (115/148) had some epilepsy specialist nurse (ESN) provision; 85.8% (127/148) had a defined epilepsy clinic seeing patients at secondary level. 92.6% (137/148) of HB/T had agreed referral pathways to tertiary paediatric neurology services. Satellite paediatric neurology clinics were hosted in 77.0% (114/148) of HB/T.
Conclusions: There are improvements in the overall numbers of epilepsy nurse specialists, paediatricians with expertise and specific clinics for children and young people with epilepsies. The findings led to comprehensive recommendations to HB/T and commissioners, informed updates to the epilepsy best practice tariff and themes within the NHS Long Term Plan.

Poster No. 008
Diagnosing and managing seizures on PICU: an explanatory sequential mixed methods approach

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Aims: To investigate the views of health care professionals on the challenges faced in diagnosing and treating seizures on PICU and the role of brain function monitoring.
Methods: An explanatory sequential mix methods approach (QUAN→QUAL) with equal weighting between stages. We collected qualitative data via a questionnaire sent to all UK PICU units. The questionnaires were used to identify 13 members of staff for semi-structured interviews. Thematic analysis was used to interpret the qualitative data.
Results: 72 questionnaire responses were collected: 48.6% PICU nurses, 20.8% consultants, 20.8% advanced nurse practitioners and 5.6% other members of staff. 13.0% responders thought seizures were easy and 71.0% hard to diagnose on PICU. 81.1% had seen misdiagnosis of seizures. 39.7% used some form of neurophysiological monitoring on PICU, of whom 44.0% used amplitude integrated electroencephalography. Thematic analysis showed that PICU staff need to feel in control of their patients, and difficulty in diagnosing seizures left staff feeling out of control and anxious. Suggested reasons for diagnostic difficulty included: a lack of training on seizure semiology, sedative or paralysing drugs, lack of experienced staff to ask for an opinion, not knowing the child's background neurological state or seizure type, and the parents not being present. Cerebral function monitoring was considered a way of improving diagnosis, reducing ambiguity and raising the confidence of PICU staff. A small number of staff preferred not to monitor patients because it was not clear treating seizures without clinical features improved outcome.
Conclusions: Health care professionals on PICU need to feel in control of their patents, and difficulties in diagnosing and treating seizures accurately causes ambiguity and concern. Most PICU staff want cerebral function monitoring to improve the accuracy of diagnosis and treatment, but future work is needed to show improved accuracy and treatment improves outcome.

Poster No. 009
PCDH 19 epilepsy (a rare but recognisable genetic epilepsy syndrome): our experience with three female siblings

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Aim: To report three cases of Protocadherin 19 related epilepsy in three female siblings with familial inheritance.
Cases: 1st Child: 5 years 8 months old sibling developed seizures at 10 months with cluster of brief tonic seizures associated with staring; clonic and a few prolonged generalised

tonic clonic seizures. Awake and Sleep EEG showed temporal focal slowing. She was labelled as non lesional focal epilepsy after a normal MRI scan and was discharged on Keppra. She had multiple admissions with cluster of brief seizures at the age of 12, 16, 25, 26, 34, 38 and 46 months associated sometimes with febrile illness with poor response to intravenous AED's. She was diagnosed with autism at 42 months. 2nd Child: 38 months old younger sibling had seizure onset at 9 months. Seizures were tonic in nature, brief, multiple and in clusters over a period of 2 to 3 days. EEG's showed non-specific slowing during seizures. Array cGH revealed chromosome 3p26.1 microdeletion. Keppra was commenced and increased but recurrent cluster of seizures at the age of 15, 19 and 24 months required admission with poor response to IV AED's. Family history revealed that half-sister (biological father's daughter who had epilepsy and global developmental delay) was diagnosed with PCDH 19 epilepsy. Gene tests were requested on both siblings and both were heterozygous for PCDH 19 mutation. She had delayed social and communication skills from 2 years with a diagnosis of Autism at 30 months. 3rd Child: 1 year old half sibling (father's 4th child from 3rd relationship) has tested positive for PCDH 19. Her development is normal and so far there have been no seizures.

Conclusions: PCDH 19 epilepsy is increasingly recognised as one of the early onset infantile encephalopathies. Gene testing is likely to yield a diagnosis with a family history or with a typical phenotype.

Poster No. 010
Seizure, developmental and cognitive outcomes in children post hemispherotomy

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Introduction: Patients with focal refractory epilepsy secondary to structural hemispheric changes have been shown in retrospective studies to have significantly improved seizure outcomes following hemispheric disconnection. The aim of this study was to report the seizure and cognitive outcomes in our cohort and investigate prognostic factors for seizure outcomes.

Methods: This was a single-centre retrospective study on children and adolescents who had hemispherotomy for refractory epilepsy in the Royal Manchester Children's Hospital between 2008 and 2017.

Results: Twenty-two patients were included with median (range) age of seizure onset and of surgery of 4 (0–168) and 72 (13–217) months respectively. Median (range) time from seizure onset to surgery was 38.5 (12–172) months. The most common aetiologies were antenatal/perinatal middle cerebral artery infarct (n=6) and malformations of cortical development (n=6). At 1 year after surgery and at last follow-up (median [range] 38 [2–107] months), 50% (10/20) and 32% (7/22) achieved complete seizure freedom. The number of anti-epileptic medications decreased for 10 (45%) at last follow-up. Lateralisation of ictal and interictal EEG (p=1.00, p=0.11), aetiology (p=0.75), age of first seizure (p=0.45) were not associated with seizure recurrence. Five who had formal neuropsychological testing using the Wechsler Intelligence Scale for Children (WISC) showed improvement in cognitive abilities across all subsets post-surgery. Ten children showed reduction in median Vineland Adaptive Behaviour score, from 58 to 49.5, indicating a failure to progress rather than regression of skills. Nine (45%) had newly reported behavioural or psychiatric issues including sleeping problems, challenging behaviours, autistic spectrum disorder. Sixteen (84%) were reported by parents/carers to show improved verbal abilities postoperatively while the rest had unchanged verbal abilities.

Conclusions: We present a cohort of children with early onset seizures who had hemispherotomy at a relatively early age. Our cohort showed good seizure outcomes and cognitive improvements. There were no prognostic factors for seizure outcome identified in this small group.

Poster No. 011
The MRI phenotype of ATP1A3-related disease

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Objective: ATP1A3 mutations cause a spectrum of rare neurological phenotypes, including Alternating Hemiplegia of Childhood (AHC) and Cerebellar Ataxia, Pes Cavus, Optic atrophy and Sensorineural hearing loss (CAPOS) syndrome. There are indications that clinical phenotypes are mutation-specific, but little is known about MRI phenotypes. We wanted to investigate whether deep neuroimaging phenotyping reveals phenotype-specific MRI features of ATP1A3-related disease.

Methods: We re-examined MRI data of 13 patients with confirmed ATP1A3-related disease and associated findings with ATP1A3 mutation and clinical phenotype.

Results: Six patients had a phenotype of AHC, 3 CAPOS, 1 Relapsing Encephalopathy and Cerebellar Atrophy, 1 Early Epileptic Encephalopathy and 2 intermediate phenotypes. MRIs were obtained at a median of 6 years (min=0.5, max=13, IQR=1–10). Ten MRIs had been previously reported normal. On re-examination, with a focus on subtle condition-specific features, 12 (92%) patients showed abnormality of the corpus callosum, 9 (69%) of the cerebellum, 2 (15%) of the pons, 2 (15%) had delayed myelination and 2 (15%) generalized cerebral atrophy. All patients (100%) with the CAPOS specific mutation p.E818K showed a consistent MRI phenotype of mildly thickened corpus callosum, optic atrophy and superior cerebellar atrophy, consistent with their clinical phenotype. In

contrast, all AHC patients with MRI abnormalities (83%) had a hypoplastic corpus callosum. The only patient with normal MRI was the patient carrying mutation p.G497R, associated with a mild clinical phenotype. Of the patients with clinical ataxia (*n*=7), 5 (71%) had cerebellar atrophy on MRI; 2 patients with cerebellar atrophy were not ataxic. Two (67%) of the 3 patients with severe intellectual disability had cerebral atrophy.
Conclusions: ATP1A3 mutations have subtle radiological findings, clustering around callosal dysmorphisms, as well as pontine and cerebellar abnormalities that seem to form distinctive MRI phenotypes for AHC and CAPOS. Study of larger cohorts is required to more accurately define mutation-specific phenotypes and allow for quantitative analysis.

Poster No. 012

Long-term safety and efficacy of adjunctive perampanel in paediatric patients (aged 4 to <12y) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS) in Study 311

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Objective: Study 311 (NCT02849626) was a multicentre, open-label, single-arm study of perampanel oral suspension (0.5mg/mL) in paediatric patients (aged 4 to <12y) with POS (with/without secondarily generalised seizures [SGS]) or PGTCS. Here, we report long-term (1y) safety and efficacy data of adjunctive perampanel in paediatric patients from Study 311.
Methods: This analysis included cumulative data from all enrolled patients in the Core Study (23wks of treatment) and Extension Phase A (52wks of treatment). Assessments included monitoring of treatment-emergent adverse events (TEAEs), median percent change in seizure frequency per 28 days from baseline, and 50% responder and seizure-freedom rates.
Results: Of 180 patients enrolled in the Core Study (POS, *n*=149; SGS, *n*=54; PGTCS, *n*=31), 136 patients entered Extension A. Of these, 14 patients discontinued Extension A; most common primary reasons for discontinuation were adverse events (3.7%) and inadequate therapeutic effect (2.9%). For all patients, mean (standard deviation [SD]) time since diagnosis was 5.7 (2.9) years and mean (SD) duration of exposure was 41.5 (17.3) weeks. During baseline, 55.6% of patients received two concomitant anti-seizure medications. TEAEs were reported in 162 (90.0%) patients; somnolence was the most commonly reported (27.2%). Median percent reductions in POS, SGS and PGTCS frequencies at Weeks 1–13 were 43.0%, 57.9% and 79.3%, respectively; these were maintained at Weeks 40–52 and were 69.4%, 73.8% and 100.0%, respectively. Seizure-freedom rates for POS, SGS and PGTCS at Weeks 40–52 were 13.0%, 24.4% and 38.5%, respectively.
Conclusions: Long-term (1y) adjunctive perampanel is generally safe, well tolerated and efficacious in paediatric patients aged 4 to <12 with POS (with/without SGS) or PGTCS.

Poster No. 013

Long-term adjunctive perampanel and health-related quality of life (HRQoL) in paediatric patients (aged 4 to <12y) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS): study 311

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Objective: Study 311 (NCT02849626) was a multicentre, open-label study of adjunctive perampanel oral suspension in paediatric patients (aged 4 to <12y) with POS (with/without secondarily generalised seizures [SGS]) or PGTCS. We report long-term (1y) HRQoL data using the EuroQol 5 Dimensions-Youth (EQ-5D-Y) scale from Study 311.
Methods: This analysis included cumulative data from all enrolled patients in the Core Study and Extension Phase A (23 and 52wks of treatment, respectively). EQ-5D-Y was assessed at baseline, Week 23 and Week 52, and included five domains (mobility, self-care, doing usual activities, pain/discomfort, feeling worried/sad/unhappy). The EQ-5D-Y visual analogue scale (VAS) was also assessed; increases in VAS correspond with improvements. Data are for observed cases.
Results: All 180 enrolled patients were included in the EQ-5D-Y analyses. The proportion of patients reporting 'a lot of problems' was similar during baseline vs Week 52: mobility, 20/112 (17.9%) vs 13/68 (19.1); self-care, 44/112 (39.3%) vs 23/68 (33.8%); doing usual activities, 27/112 (24.1%) vs 18/68 (26.5%); pain/discomfort, 4/115 (3.5%) vs 2/70 (2.9%); feeling worried/sad/unhappy, 4/113 (3.5%) vs 1/70 (1.4%). Outcomes were also similar for 'no problems' during baseline vs Week 52: mobility, 64/112 (57.1%) vs 43/68 (63.2%); self-care, 42/112 (37.5%) vs 27/68 (39.7%); doing usual activities, 53/112 (47.3%) vs 34/68 (50.0%); pain/discomfort, 78/115 (67.8%) vs 50/70 (71.4%); feeling worried/sad/unhappy, 80/113 (70.8%) vs 52/70 (74.3%). Mean (standard deviation) change in EQ-5D-Y VAS from baseline at Week 52 was 5.1 (16.6).
Conclusions: Long-term adjunctive perampanel treatment (up to 1y) does not negatively affect HRQoL (based on all EQ-5D-Y domains) in patients aged 4 to <12 years with POS (with/without SGS) or PGTCS.

Poster No. 014

Efficacy and safety of adjunctive perampanel for partial-onset seizures (POS) in adult, adolescent and paediatric populations (Studies 304, 305, 306, 311)

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Objective: Here we present efficacy and safety data of adjunctive perampanel for POS from Phase III studies in adolescent/

adult patients (aged ≥12 years; Studies 304 [NCT00699972], 305 [NCT00699582] and 306 [NCT00700310]), and paediatric patients (aged 4 to <12y; Study 311 [NCT02849626]) with POS (with/without secondarily generalised seizures [SGS]).
Methods: Across Studies 304, 305 and 306, 1480 patients received placebo or perampanel 2–12mg/day (19-week Treatment Period). In Study 311, 149 patients received perampanel ≤12mg/day (without enzyme-inducing anti-seizure medications [EIASMs]) or ≤16mg/day (with EIASMs) (23-week Treatment Period). Efficacy assessments included median percent change in seizure frequency/28 days from baseline, 50% responder rate and seizure-free rate. Safety assessments included the incidence of treatment-emergent adverse events (TEAEs).
Results: The median percent reduction in seizure frequency/28 days was greater with perampanel at 4 (23.3%), 8 (28.8%) and 12mg/day (27.2%) vs placebo (12.8%; $p<0.01$) in adolescent/adult patients and was 40.1% in paediatric patients. The 50% responder rate during the Maintenance Period was greater with perampanel at 4 (28.5%), 8 (35.3%) and 12mg/day (35.0%) vs placebo (19.3%; $p<0.05$) in adolescent/adult patients and was 46.6% in paediatric patients. Seizure-freedom rates were greater with perampanel at 4 (4.4%), 8 (3.5%) and 12mg/day (4.1%) vs placebo (1.0%; $p<0.05$) in adolescent/adult patients and was 11.5% in paediatric patients. TEAEs occurred in 61.7%–89.0% of adolescent/adult patients with perampanel 2–12mg/day (vs 66.5% in placebo patients), and in 89.9% of paediatric patients. TEAEs observed in pediatric patients were similar to those reported in adolescents and adults.
Conclusions: These studies suggest perampanel is efficacious and generally safe in paediatric, adolescent and adult patients with POS (with/without SGS).

Poster No. 015
Long-term safety and efficacy of cannabidiol (CBD) treatment in patients with Lennox-Gastaut syndrome (LGS): 3-year results of an open-label extension (OLE) trial (GWPCARE5)

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Objective: To assess long-term safety and efficacy of add-on CBD in patients with Lennox-Gastaut syndrome (LGS) in the third analysis of the open label extension (OLE; GWPCARE5) of 2 Phase 3, randomised controlled trials (RCTs), GWPCARE3 and GWPCARE4.
Methods: Patients who completed either of the RCTs could enter this OLE trial (GWPCARE5/NCT02224573). Patients received GW Pharmaceuticals' plant-derived highly purified CBD medicine (100mg/mL oral solution). The primary endpoint was safety. The secondary efficacy endpoints were median percentage change from baseline in drop and total seizure frequency.
Results: Overall, 99% (366/368) of eligible patients with LGS entered the OLE. Median follow-up was 150 weeks (3d to 179wks); 119 patients (33%) withdrew. Mean age: 16 years; 33% ≥18 years; 54% male. Baseline median seizure frequency/28 days: 80 drop seizures; 168 total seizures. During the extended follow-up, the incidence of adverse events (AE) was 96%; serious AEs 42%; AEs leading to discontinuation 12%. Most common AEs (≥20%): diarrhoea, convulsion, pyrexia, somnolence, vomiting, upper respiratory tract infection, and decreased appetite. AEs of alanine aminotransferase increased occurred in 8% of patients. There were 11 deaths; none deemed treatment-related by the investigator(s). Median percentage reductions in seizure frequency (12-wk windows over 156wks) was 48–71% for drop seizures and 48–68% for total seizures.
Conclusions: Long-term treatment with add-on CBD in patients with LGS produced sustained seizure reductions, with no new safety concerns.

Poster No. 016
Management of status epilepticus in children with Dravet syndrome

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Objective: Status epilepticus is reported to be the second greatest cause of mortality in children with Dravet Syndrome. We aimed to review the evidence on convulsive status management in children with Dravet syndrome to guide local practice.
Methods: Literature review.
Results: PubMed search using search terms 'Dravet' OR 'SCN1a' AND 'status epilepticus' returned 149 results, of which 8 were relevant. Only one of these articles presented specific data on reported effectiveness of medications used in acute seizure management; this was based upon retrospective questionnaire data and defined status epilepticus as seizures lasting 30 minutes or longer. Here, the most efficacious agents reported to terminate such seizures within 10 minutes were intravenous barbiturates (16 of 19 patients) and benzodiazepines (60 of 102 patients). Rectal benzodiazepines, chloral hydrate and intravenous phenytoin or lidocaine were reported as less effective. The remaining articles presented expert and consensus opinion, all advising early administration (some at seizure onset) of buccal or intravenous benzodiazepines. Provision of rescue medication for home use, with individualised plans, is recommended. One author advocated giving three doses of benzodiazepines sequentially. An article summarising a consensus panel described sodium valproate as a preferred second line option where benzodiazepines are ineffective, but there was no overall agreement on other possible medications. Several articles advised caution in using phenytoin in acute seizure management. One source discusses possible harm from high dose barbiturates.
Conclusions: Status epilepticus management for children with Dravet syndrome should feature early, rapidly acting

benzodiazepine administration. For second line treatment, phenytoin and barbiturates are commonly used in 'standard' status epilepticus management protocols, but there are potentially concerns around their use in this patient group. These concerns, however, appear largely theoretical. In the absence of evidence favouring a specific management protocol, individualised care plans should be designed with involvement of patients and their carers.

Poster No. 017

ZX008 (low dose fenfluramine hydrochloride oral solution) significantly reduces frequency of generalized tonic-clonic seizures in Dravet syndrome: pooled analysis from two phase 3 clinical trials

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Objective: ZX008 (low dose fenfluramine HCl oral solution) significantly reduced the frequency of convulsive seizures in patients with Dravet syndrome (DS) in two Phase 3 clinical trials. We conducted a pooled analysis of these trials to analyze the effect of ZX008 on the frequency of tonic-clonic seizures (TCs), recently identified as a major risk factor for sudden unexpected death in epilepsy.
Methods: The frequency of generalized TCs and focal-to-bilateral TCs in patients with DS enrolled in one of two phase 3 clinical trials of ZX008 added to current antiepileptic drug regimens were analyzed.
Results: 206 patients (55% male, mean age 9y) were enrolled and randomized to placebo (n=84), or ZX008 0.8 (n=40), 0.5 (n=43), or 0.2 (n=39) mg/kg/day. The median baseline monthly frequency of generalized TCs ranged from 8.0 to 12.3/month in the four dose groups, and decreased during treatment by 80%, 64%, and 48% in the ZX008 0.8, 0.5, and 0.2mg/kg/day groups, respectively, and by 10% in the placebo group. Focal-to-bilateral TCs were experienced by fewer patients and had a median baseline frequency of 2.0 to 4.7/month. During treatment, median percentage reductions in focal-to-bilateral TC frequency were 97%, 33%, and 69% in the ZX008 0.8, 0.5, and 0.2mg/kg/day groups, respectively, and 39% in the placebo group. Most common adverse events included decreased appetite, diarrhea, and fatigue. No valvular heart disease or pulmonary arterial hypertension was seen in any participant at any time.
Conclusions: ZX008 substantially reduced the frequency of TCs. ZX008 may be an important, effective new treatment option for DS patients.

Poster No. 018

TBC1D24 mutations are a newly recognised cause of paroxysmal exercise-induced dystonia

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Objective: Mutations affecting TBC1D24 have been associated with an expanding spectrum of phenotypes including developmental delay, hearing impairment, DOORS syndrome and a range of epilepsies. A number of different movement disorders, including ataxia, spasticity and episodic paroxysmal dystonia have also been described. Here we report two unrelated patients with biallelic TBC1D24 variants, in whom exercise-induced dystonia was a major disease feature.
Methods: Both patients were diagnosed through whole-exome sequencing. Clinical information was obtained by a review of the medical notes, clinical correspondence and available video footage.
Results: Both patients were found to have compound heterozygous mutations in TBC1D24, associated with an episodic dystonic/dyskinetic movement disorder reliably triggered by exertion. In the case of Patient 1, exertion of specific body parts induced specific localised symptoms: for example, singing would precipitate orolingual dyskinesia. Both girls experienced truncal dystonia – specifically, lateral flexion of the trunk – brought on by prolonged walking. Both girls also had epilepsy; of note, the exercise-induced movements and postures were captured on EEG and had no ictal correlate.
Conclusions: Although TBC1D24 mutations are an established genetic cause of epilepsy, our study further confirms that not all paroxysmal events in people with TBC1D24 mutations are epileptic in nature. TBC1D24 should be included in the genetic differential diagnosis of patients with complex neurological syndromes associated with paroxysmal exercise-induced dyskinesia.

Poster No. 019

RHOBTB2 mutations cause a range of episodic movement disorders as well as epilepsy

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Objectives: Heterozygous de novo RHOBTB2 mutations have recently been reported in developmental and epileptic encephalopathy, but the associated movement phenotypes are not fully delineated. In order to better define the expanding phenotype and movement disorder in RHOBTB2-related disease, we report a series of 9 unrelated patients presenting with complex movement disorders as well as epilepsy and developmental impairment.

Methods: Cases were identified both in the UK (through the neurogenetic services at Great Ormond Street Hospital and the National Hospital for Neurology and Neurosurgery, London), and from international collaborating centres. Data were collected retrospectively by the patients' clinicians, using a standardised proforma.

Results: Nine individuals were identified, aged from 2 to 55 years. 8/9 had epilepsy. Of these, 4/8 had achieved seizure freedom at their last review. The commonest seizure types were focal onset with impaired awareness and/or focal to bilateral tonic-clonic seizures. 7/9 also had a paroxysmal movement disorder, which included hemiplegic or asymmetrical episodic weakness in 5/7, generalised dyskinesia in 4/7, episodic focal dystonia in 3/7 and episodic ataxia in 3/7. All individuals affected by a movement disorder had at least two different types of episodes. Movement disorders improved significantly after treatment with carbamazepine in three children. Cognitive ability varied from average to severe intellectual disability and in all but one case, developmental delay predated the onset of epilepsy.

Conclusions: RHOBTB2 mutations cause a complex neurological phenotype associated with both epileptic and non-epileptic paroxysms. Paroxysmal events occurring in people with known RHOBTB2 mutation should therefore not be assumed always to be epileptic in nature. Our study confirms that a wide variety of movement disorders are reported, including some which fall within the spectrum of alternating hemiplegia of childhood (AHC). RHOBTB2 should thus be considered as a potential gene for AHC, other complex movement disorder phenotypes and epilepsy-dyskinesia syndromes.

Poster No. 020

Evaluating seizure recognition and the use of electroencephalography in the paediatric intensive care unit

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Objective: In the paediatric intensive care unit (PICU), seizures are challenging to detect given patient complexity, comorbidity and sedation. This has led to both over- and under-treatment of seizures. There is growing literature on the use of continuous electroencephalography in PICU, considered gold standard but not universally available, but little on standard electroencephalography (EEG).

This study aims to investigate the indications for EEG requests, their efficacy and the use of antiepileptic drugs (AED) in PICU, hypothesising a difficulty in clinically differentiating between epileptic and non-epileptic events and suboptimal use of AEDs.

Methods: This retrospective study examined EEG reports over 2 years at a tertiary PICU. Data was collected on participant characteristics, EEG indications and findings and AED use.

Results: 185 EEG reports from 142 participants were included. Median age was 6 months (IQR 1mo–3y 6mo). Indications for EEG (often multiple per EEG) included suspected clinical seizures (64%), suspected subclinical seizures (21%), prognostication (28%) and suspected encephalopathy (8%). 63% of participants with suspected seizures were sedated and 43% of all participants were encephalopathic. Clinical episodes suspected to be seizures were captured in 41/141 EEGs. Only 22% of these were EEG-confirmed seizures. Captured movements shown not to be seizures are qualitatively described. 6% of patients with suspected seizures had electrographic seizures with no clinical correlate. Most confirmed seizures were in participants without pre-existing epilepsy. Antiepileptic(s) were changed prior to 25/35 captured events. Seizures were present in 28% of these cases, while 60% had neither clinical nor electrographic seizure activity. 7/8 participants with confirmed clinical seizures had AEDs changed.

Conclusion: It is challenging for clinicians to differentiate between seizure and non-seizure movements in PICU. Moreover, there are issues of over-medication and low event-capture rate with EEG. We propose a multidisciplinary education strategy and investment in cEEG to address these issues.

Poster No. 021

The spectrum of GLUT1-DS and use of ketogenic diet Royal Manchester Children's Hospital 2004–2019

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Introduction: Glucose Transporter 1 deficiency syndrome (GLUT1-DS) is a rare neurometabolic disorder causing

impaired glucose transport into the brain. In the majority of patients, it is caused by an autosomal dominant heterozygous mutation in the SCL2A1 gene. Ketone bodies generated by a ketogenic diet (KD) provide the brain with an alternative energy source and is gold standard therapy. We report our experience for our cohort of patients at Royal Manchester Children's Hospital.

Methods: Retrospective case note review of 14 patients with GLUT1-DS at Royal Manchester Children's Hospital from 2004 to 2019.

Results: 14 patients – 8 male, 6 female. Age range 3 to 19 years. Average age at diagnosis was 6 years 3 months (range 4mo–9y). There was a history of seizures in 11 of 14 patients with average seizure onset of 2 years 6 months. Seizures types were absences (5/11), generalised tonic-clonic (3/11), myoclonic (2/11), myoclonic astatic (1/11), tonic (1/11) and focal to bilateral tonic-clonic (1/11). Ketogenic diet was used in all patients for a range of 4 months to 10 years 7 months. No significant adverse effects occurred that required discontinuation. Six patients complying with KD are seizure free and not taking antiepileptic drugs (AEDs). One of these patients had occasional tonic-clonic seizures with illness and loss of ketosis but has been seizure free for >18 months. Five patients are non-compliant with KD – two have good seizure control with AEDs, potentially limiting motivation, and two (siblings) have a parent with GLUT1-DS and learning difficulties. Learning difficulties were reported in 10 patients. Other symptoms included ataxia (8/14), dysarthria (5/14), tremor (4/14) and dystonia (4/14). One patient presented with episodic hemiplegia.

Conclusions: Patients with GLUT1-DS are a heterogeneous group leading to challenges in diagnosis, management and prognosis. Ketogenic diet has been effective in managing this cohort but compliance was a limiting factor.

Poster No. 022
Survey of management of epilepsy relapse in children in East of England (EOE)

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Objective: To conduct a survey regarding the management of relapse in children epilepsy in following weaning off AEDs.

Methods: We conducted an online survey in the East of England (EOE) via the Eastern Paediatric Epilepsy Network (EPEN) regarding the management of relapse in children epilepsy after weaning AEDs. EPEN is a network of paediatricians and nurse specialist with EOE who manage lead in management children with epilepsy within all the DGH's in the region. The questions in the survey asked about various aspects of management of patients after relapse, including the choice of anti-epileptic medication restarted, if started, any further investigations undertaken, and finally, the length of AED treatment before a second attempt at weaning might be considered.

Results: We received 17 responses from paediatricians in 16 DGH's across EOE. There was a large degree of variation in the responses to all of the questions in the survey. The frequency and semiology of seizures on relapse seemed to play a key role in decision making, as did the thoughts and views of the family and patient themselves. It was interesting to note there was a variation in response to whether any further investigations would be undertaken and if these were deemed necessary. Most clinicians responded that they would continue AEDs for another 2 years before attempting weaning again.

Conclusions: There is variability in the management of epilepsy relapse in the EOE and we suspect that this may also be the case nationally. To investigate this further, we would envisage extending the survey nationally, via OPEN UK – which is an organisation that links the various regional paediatric epilepsy networks across UK. This would enable establishing a standardized guideline for management of epilepsy relapse in the future.

Poster No. 023
DHDDS related developmental and epileptic encephalopathy – familial as well as sporadic

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Objective: De novo dominant mutations in DHDDS were recently identified as a cause of developmental and epileptic encephalopathy. DHDDS encodes dehydrodolichyl diphosphate synthase, which is essential for dolichol monophosphate synthesis and protein glycosylation. We report two half-siblings with a new pathogenic, maternally inherited DHDDS missense variant, c.614G>A(p.Arg205Gln), identified through whole-exome sequencing.

Method: Case note and literature review.

Results: Sibling 1, aged 11 years, presented at 11 months with global developmental delay, hypotonia and frequent absences with eyelid myoclonia. From age 3, she developed atonic drop attacks, myoclonic seizures, tremor, ataxia and facial dyskinesia. Dyskinesia and mobility deteriorated from age 7 and she is now largely non-ambulant. Severe learning disability with possible cognitive deterioration and insatiable appetite are also features. Sibling 2, aged 9 years, developed blank spells associated with eyelid flickering at 12 months and atonic drop attacks aged 5. Development delay is present, but progress is greater than her sibling. Dyskinesia, tremor, ataxia and deterioration in mobility are features. Neither is dysmorphic. EEGs on both showed bursts of irregular generalised spike wave associated with head nods and eyelid flutter. Photosensitivity was not shown but both were treated with anti-epileptic medication. MRI scans are normal. Clobazam and zonisamide improved seizure control in both. Mother has mild learning difficulties, tremor and dyspraxia. She had generalised tonic clonic seizures, from age 14 to 18 years, well controlled with lamotrigine. Compared to the six known cases in the literature, our report confirms atonic seizures and dyskinesia as important features of this disorder, in addition to common characteristics of myoclonic component to seizures, hypotonia and tremor. Learning disability is of variable severity.

Conclusions: This is the first report of familial inheritance of DHDDS related developmental and epileptic encephalopathy and describes variable severity of the phenotype within family members. The features described are consistent with those previously observed.

Poster No. 024
Duration of treatment on the relapse rate in childhood absence epilepsy (CAE) and the use of the EEG as a prognostic tool

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Objectives: To evaluate whether the duration of treatment has an effect on the relapse rate in children with CAE attending a Paediatric Neurology Centre in Cyprus, and whether the EEG can be used as a prognostic tool.
Methods: Electronic patient database review of patients with CAE, who have discontinued treatment attending the paediatric neurology clinic between years 2008–2017.
Results: Fourteen patients with CAE, off treatment were identified (7 male). Age at presentation ranged from 3 to 9 years (median 6.5y). All patients underwent an EEG to confirm diagnosis and those who presented with seizures other than absences were excluded. Twelve patients were treated with Valproic acid (Depakine) and 2 with Ethosuximide (Zarontin). In 10, absences resolved on first line monotherapy, whilst 4 were refractory requiring combination therapy. Positive family history was present in 2 (non–identical twins), attention deficit in 2, and learning difficulties in 1 patient. All initial EEGs were consistent with CAE, patients also underwent an EEG post seizure control to confirm resolution. Mean time to seizure cessation was 3.9 months, mean duration of treatment 2.2 years; 4 patients discontinued treatment after 1 year of seizure freedom. Prior to withdrawing treatment all patients had an EEG (normal 6, mildly abnormal with brief generalised discharges 6, photosensitivity 1, brief electrographic absence 1). Relapse occurred in 3 patients who required re-instigation of treatment. Mild abnormalities on EEG prior to coming off treatment did not correlate with a higher relapse rate. There was no difference in relapse rate in patients on treatment for 1, 2 or more years. Patients were followed up for a mean of 7.8 years.
Conclusions: Treating patients with CAE for less than 2 years does not affect relapse rate provided patients are seizure free, also confirmed by EEG normalisation, which may be used as an additional predictor.

Poster No. 025
Rare-case report, UNC80 gene mutation with microcephaly

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Background: Mutations in UNC80, Encoding Part of the UNC79-UNC80-NALCN Channel Complex, Causes Autosomal-Recessive Severe Infantile Encephalopathy, this is a rare case of profound global developmental delay with psychomotor retardation. Only 19 individuals have been reported to date. UNC80 deficiency is characterized by hypotonia, strabismus, oral motor dysfunction, postnatal growth deficiency, and developmental delay. The majority of individuals do not learn to walk. All individuals lack expressive language. Additional features can include nystagmus, extremity hypertonia, a high-pitched cry, repetitive and self-stimulatory behaviours, constipation, clubfeet, joint contractures, and scoliosis. There is no loss of skills suggestive of neurodegeneration.
Case presentation: 11-year-old, with a recent confirmed diagnosis of UNC80 gene mutation and microcephaly. She had Profound global developmental delay, learning disability, bilateral squint with cortical blindness, seizure disorder, sleep apnoea, Head drops, movement disorders, feeding difficulty, scoliosis and constipation. Term baby with normal anti-natal history. Induction of labour for IUGR. Good APGAR, at birth but developed Respiratory distress with Cardiac problems. Birth weight 2050 g. Neurologically: Floppy with reduced muscle tone and microcephaly. Had a short neonatal admission and discharged with cardiac, endocrine, neonatal and neurodevelopmental delay follow-up. She had no spoken words and communicated by crying. She was only able to sit transiently and never walked. She was wheelchair bound with GMFCS, MACS, CFCS and EDACS level 5 each, needing full 24-hour support from patents and carers. DDD study confirmed UNC80 Gene Mutation, her cousin was also noted to have same gene mutation via exome sequencing and with similar clinical picture.
Conclusion: Early diagnosis is key for genetic counselling for further children and ensuring global support as reported individuals span ages from birth to 15 year. The diagnosis is established in a pro-band with developmental delay and hypotonia by identification of bi-allelic pathogenic variants in UNC80 on molecular genetic testing.

Poster No. 026
Cognition and disease burden in SCN1A positive Dravet syndrome – a 10-year follow-up study

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Objective: Dravet syndrome (DS) is caused by a mutation in the SCN1A gene and results in severe epilepsy and intellectual disability. We aimed to investigate the longitudinal cognitive

development, disease burden and sleep profile of patients with Dravet syndrome.
Methods: This is a follow-up to a 2009 study previously involving 141 DS patients with detailed developmental and clinical information available. Participants completed a structured postal questionnaire on epilepsy severity and disease burden, the Adaptive Behavioural Assessment System (ABAS-3), the Sleep Disturbances Scale for Children, Pediatric Quality of Life Inventory (PedsQL) and the Strength and Difficulties Questionnaire.
Results: 123/141 from the original cohort were contactable and 70 (57%) of carers completed the outcome measures. The developmental quotient at follow-up was significantly lower compared to the earlier study (p=0.001), and 89% of affected individuals had a severe or profound learning disability. We observed the steepest decline in cognitive functioning in those that were youngest (age 0–5y) at original study onset (p=0.001).

Poorer developmental quotients correlated with early onset of initial developmental concerns (rS=0.31; p=0.037), later mobility problems (rS=0.30; p=0.015), higher levels of behaviour problems (rS=0.26; p=0.043) and worse PedsQL scores (rS=0.31; p=0.015). Carers health and wellbeing was negatively affected in 98% of cases and in 90%, at least one of the two carers quit their job due to their child's illness. Sleep problems as measured by total sleep scale score were reported in 40% of patients, whilst 71% had at least one abnormal sleep scale category. Only 49% of individuals with abnormal sleep scores received treatment. rS=Spearman rho correlation coefficient.
Conclusions: This study highlights the ongoing cognitive decline in DS, particularly affecting younger patients, alongside often untreated sleep problems and a significant disease burden on primary carers. With new therapeutic opportunities on the horizon, early interventions appear crucial to avert the observed severe cognitive decline.

Poster No. 027
Forced normalisation as a factor in behaviour deterioration on the ketogenic diet

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Introduction: There have been a number of reports that demonstrate a correlation between improved seizure management and deterioration of behaviour with psychosis in adults and children. Forced normalisation is a concept where there is deterioration in behaviour when better seizure control is achieved with antiepileptic drugs (AEDS) or epilepsy surgery. The Ketogenic Diet (KD) is a treatment option for children with refractory epilepsy with approximately 50 to 60% showing at least 50% reduction of seizures and 15% of those patients reaching seizure freedom 6 months after treatment. Although forced normalisation has been discussed in literature following AEDS and neurosurgical interventions, it has not been reported following the use of KD.
Cases: Of the 195 children that have commenced on KD over the last 7 years at Royal Manchester Children's Hospital, 59.5% responded to the diet (at least 50% improvement in seizures) and 10.8% were non-compliant.

We present 6 patients under the care of the KD service, whose behaviour deteriorated on KD when seizure reduction was >50%. The behaviour changes described by parents included poor sleep, unsettled, agitation, head-banging and shouting. Five out of the six patients stopped KD treatment, with subsequent improvement in behaviour.
Conclusions: There are reports that patients on the ketogenic diet with seizure freedom show improvement in their behaviour, unlike our small cohort whose behaviour deteriorated. Forced normalisation has been explored in paediatric patients as a cause for behaviour deterioration following surgical and medical management for intractable seizures. The associated factors of deteriorating behaviour have not yet been explored in depth with the ketogenic diet.

Poster No. 028
Clinical audit of lacosamide in children and young people

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Objective: We wanted to determine how lacosamide was being used in children locally, and what their outcomes were at a year.
Methods: We undertook a registered, retrospective, clinical audit using hospital electronic records. We ascertained every patient aged <18 years who had been dispensed lacosamide January 2016- January 2018. The electronic health records were reviewed, and data collected using a standard proforma, including: patient demographics, age of seizure onset, seizure type, ECG and MRI findings, baseline seizure frequency, seizure frequency 2, 6, and 12 months on lacosamide, maximum dose prescribed (mg/kg/day), and adverse effects at 2, 6, and 12 months.
Results: 20/42 (48%) patients were male, the median age was 9 years (range 2mo to 17y), with a mean age of onset of 3 years (range 2mo to 11y). 35/42 (83%) had epileptiform activity on EEG and 24/42 (57%) had an abnormal MRI. 24/42 (57%) had focal seizures. 27/42 (64%) had a minimum of one seizure a week. 28/42 (66%) had previously tried 3 or more antiepileptic drugs (AEDs), and 38/42 (90%) had drug resistant epilepsy prior to starting lacosamide (already failed 2 previous AEDs). All patients had lacosamide alongside another AED. The mean daily dose of lacosamide was 7.3mg/kg/day (range 1.3–20.6). At 12 months, 15/42 (36%) of patients reported a >50% reduction in seizure frequency. 36/42 (86%) remained on lacosamide 1 year after starting, and 9/42 (21%) experienced an adverse side effect.
Conclusions: In this local audit, lacosamide was mostly prescribed for drug resistant epilepsies and was used in polytherapy. A third of patients saw a significant reduction in seizure frequency on lacosamide, although some were also started on other treatments during this period. Most patients remained on lacosamide after 12 months, and about 1 in 5 experienced one or more adverse side effect.

Poster No. 029
CACNA1a variant presenting as infantile onset downbeat nystagmus

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CACNA1a is a large gene which encodes for the alpha subunit of a neuronal ion channel and it is expressed widely throughout the central nervous system (CNS). Pathogenic variants in this gene have been associated with many phenotypes. Most commonly episodic ataxia type 2 (EA2) and spinocerebellar ataxia type 6 (SCA6). Rarer phenotypes include, familial hemiplegic migraine, paroxysmal tonic upgaze, epilepsy, and intellectual disability with autism. Here we present the case of an 8 month old girl who presented with new onset paroxysmal abnormal eye movements during an intercurrent illness. The referring clinicians felt these episodes may be epileptic. However, an electroencephalogram (EEG) captured these movements which were non-epileptic downbeat nystagmus. All other initial investigations including cerebrospinal fluid glucose and neurotransmitters were normal as was her neuroimaging. Over the next year her nystagmus became constant. She had otherwise normal development. At 16 months her gait was noted to be abnormally unsteady and broad based (even accounting for age). The nystagmus and ataxia changed in severity from day to day, she could have 4 to 5 more severe days followed by 4 to 5 better days, they never completely resolved. She had no family history of abnormal eye movements or ataxia. Subsequent genetic testing revealed a CACNA1a c.3787G>A p(Glu1263Lys) missense variant described only twice previously in EA2, both with very different phenotypes to our patient. Neither of her parents carried the same genetic variant. This case is the first reported case of this CACNA1a variant presenting as downbeat nystagmus followed by ataxia. Both her age of presentation and her initial presenting features are very different to the typical phenotypes associated with this gene. It broadens the phenotype of CACNA1a, and also broadens the differential diagnoses associated with abnormal eye movements in infancy. The importance of following up as yet undiagnosed patients who may go on to develop new and revealing symptoms is highlighted.

Poster No. 030
Parental/carer perception and recall of safety advice provided at epilepsy diagnosis

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Objective: To undertake a questionnaire-based survey retrospectively exploring parents'/carers' recall of, and views on, the safety and risk advice given at the time of their child's epilepsy diagnosis.
Methods: Questionnaires were distributed throughout Scotland via Scottish Paediatric Epilepsy Network (SPEN). Parents'/carers' of 5 to 12-year-old children were asked to complete the questionnaire prior to their seizure clinic appointment.
Results: 178 questionnaires were suitable for inclusion. Seizure burden was evenly distributed: 37% <1 seizure/month, 23% >1 seizure/month, 22% >1 seizure/week and 18% had absences only. Respondents could recall post-diagnosis information being provided on: water safety (50%), taking medication regularly (91%), sports/activities (57%), seizures in sleep (62%), first aid (78%), prolonged seizures (53%) and/or SUDEP (45%). There was no statistically significant difference in the duration of epilepsy diagnosis between those who could recall information being given (M=3.77y, SD 2.747) and those who could not (M=4.138y, SD 2.84; *t* test p=0.42). The majority of information was given via clinic discussions (75%). 46% received written information, 28% directed to websites and/or independent search (12%). Most information was 'just right' (71% water safety, 94% on taking AED regularly, 68% on sports/activities, 68% on seizures in sleep, 83% on first-aid for seizures). Approximately 30% of respondents want more information on seizures in sleep, water safety and sports/activities. 46% of respondents felt worried following information about seizures in sleep, 57% about prolonged seizures and 67% regarding SUDEP.
Conclusions: A substantial proportion of parents'/carers' do not recall receiving safety information on epilepsy despite this being standard practice through SPEN. This appears to be unrelated to the duration of their child's epilepsy. Repeated timely reinforcement may be of benefit. A high proportion of parents'/carers' felt concerned following information provided on nocturnal seizures, prolonged seizures and SUDEP. This should be recognised with support in place for further discussions.

Poster No. 031
Seizure outcome in responsive vagus nerve stimulation therapy in children and young people

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Aim: Vagus nerve stimulation (VNS) therapy is an established treatment for pharmacoresistant epilepsy. Newer responsive-VNS (rVNS) systems use ictal-tachycardia detection as a biomarker of seizure onset and automatically deliver additional stimulation on detection to abort the seizure. We reviewed the seizure outcomes in children and young people (CYP) implanted with rVNS at Great Ormond Street between 2012 to 2018.
Methods: Data were collected prospectively on 41 patients who had an AspireSR® rVNS inserted during time period of 2012 to 2018. Reduction in seizure frequency and severity, wean of medications and treatment complications or side-effects were assessed at time-points of 1 year, 18 months, 2 years and 3 years post-implantation.
Results: 41 CYP (mean age 11.9y) had rVNS inserted. At 1 year, 34% (14/41) had a positive response graded as >50% reduction in seizure frequency or severity (i.e., duration), 32%

(13) had benefit though <50% benefit, and 32% (13) of CYP were non-responders. This increased at 18 months to 41% (14/29) of children showing response >50%, a further 41% showed response 50% and only 17% (12/29) non-responders. Response was over-all sustained, with response lessening in only 2 children between 18 months and 2 years. Reduction of medication burden was achieved in 22% (9/41) (not attempted in all CYP). No patients achieved seizure freedom. Replacement of VNS from an older model to rVNS showed further benefit. Complications were infrequent: 12% (5/41). Device removal for infection was required in one child of small body size; successful replacement was possible within the year.
Conclusions: VNS is a useful treatment option for CYP with pharmacoresistant epilepsy. Seizure outcomes with rVNS in CYP are better than with standard VNS. Response is sustained. Benefit may not be seen by 1 year; therapy should be continued until at least 18 months. In our patients who responded later than 1-year, further optimisations of duty cycle and current were made. Replacement of older VNS. Devices with rVNS led to additional benefit. These findings are consistent with reported outcomes from adult series, though seizure freedom is not seen in CYP. In our centre, CYP who seemed to benefit most were those whose epilepsy was of structural aetiology and those with focal seizures, although our numbers were not large enough to assess the significance of this.

Poster No. 032
ATP1A3 mutation in twins presenting with apnoeic episodes, suspected seizures and possible dystonic events

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Objective: We report the case of monochorionic diamniotic twins presenting at the age of 5 months with infantile seizures and apnoeic episodes. The EIEE gene panel revealed a mutation in the gene ATP1A3, supporting the clinical diagnosis of Alternating Hemiplegia of Childhood (AHC).
Methods: Case Report.
Results: Twin R presented with staring episodes, eye deviation and tonic posturing of limbs. Episodes occurring mainly in clusters, affecting either side and requiring rescue medications for termination. Profound apnoeic episodes needing resuscitation were also noted. Twin S presented few weeks later with a very similar presentation. Developmentally making satisfactory progress with twin R showing only very mild delay. The Array CGH from twin R was normal. Several investigations were performed including two normal standard EEGs, a normal sleep EEG, a normal ECG, an ECHO showing a small PFO and an MRI scan demonstrating a left sided mesial temporal lobe sclerosis. Similar MRI findings were reported in twin S. Investigations such as urine organic acids and amino acids, plasma amino acids, Carnitine, Acylcarnitine, Transferrin Glycoforms, Mucopolysaccharidosis screen, Ammonia and Lactate were all normal. Pyridoxine was tried with no improvement, Levetiracetam was added and afterwards changed to Carbamazepine. Sodium Valproate was commenced eventually after an episode of prolonged clinical seizure. The EIEE gene panel revealed a de novo ATP1A3 mutation in both twins. Flunarizine was commenced following this result. A Video Telemetry managed to capture both epileptic and non-epileptic episodes in twin R. The epileptic episode was characterised solely as apnoeic episode due to a left temporal seizure activity spreading onto the opposite hemisphere which is concordant with the imaging finding of left mesial temporal sclerosis.
Conclusions: Knowledge of the ATP1A3 mutation allowed clinical correlation of a diagnosis of AHC, matching the wide clinical spectrum of AHC including paroxysmal dystonia and epilepsy.

Poster No. 033
Epilepsy in a child development centre population

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Objective: To assess all the cases in a child development centre (CDC) population with epilepsy, to enable characterisation of the caseload.
Methods: All case notes of children with an epilepsy diagnosis coded on the CDC database were retrospectively reviewed for demographic, investigation and treatment data.
Results: 67 children were identified. 27% were diagnosed before a year of age, and over half before their third birthday. 84% of patients had an EEG, and of these, 70% had an abnormal EEG. 55% had genetic testing performed, and of these, 86% had a genetic cause of their epilepsy identified. 78% had an MRI scan, and of these, 69% had a structural cause for their epilepsy identified. 90% had global developmental delay, and 90% had a diagnosis of learning disability. One third have a diagnosis of cerebral palsy, 16% have autism spectrum disorder, and 13% have a hemiplegia. 66% are seizure free, the majority of whom have their epilepsy controlled with one medication. 12% had adherence concerns identified.
Conclusions: Compared to a general paediatric epilepsy clinic, this group of children were diagnosed earlier in life, had higher rates of genetic or structural causes identified, and were less likely to be seizure free.

Poster No. 034
Sunflower syndrome: a photosensitive epilepsy with self-induced seizures

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Objective: Sunflower Syndrome is a rare photosensitive epilepsy named for sun-seeking behaviour or self-induced seizures in bright light. We highlight associated impairments, burden of self-induced seizures and treatment challenges.
Methods: Case note and literature review.

Results: Case 1. A 4-year-old with autism spectrum disorder (ASD) developed hand waving in front of her face in bright light from 3 years. Multiple myoclonic seizures occurred with screen use and her family live in complete darkness. EEG demonstrated photosensitivity, generalised spike-slow wave after hand waving and 3–3.5Hz spike-wave with myoclonia. Clonazepam has been commenced. Case 2. A 10-year-old with learning difficulties and a family history of generalised seizures presented aged 6 years with forehead rubbing leading to loss of part of her eyebrow. EEG showed photosensitivity and the generalised spike-wave of absences and eyelid myoclonia (EM). Sodium valproate was used but replaced with lamotrigine due to weight gain. Case 3. A 4-year-old with a family history of generalised seizures presented aged 2 years with hand waving in front of her face, requiring her nursery to provide a dimly-lit setting. EEG demonstrated generalised polyspike-wave, 3-Hz spike-wave and myoclonia with photic stimulation. Lamotrigine was ineffective and replaced with sodium valproate. Case 4. An 11-year-old with likely ASD developed hand waving in front of her face in bright light aged 4 years, triggering generalised tonic convulsions (GTC). She had a non-induced GTC in dappled sunlight. There was on-going anxiety and thoughts of self-harm. EEG showed photosensitivity and bursts of spikes-polyspikes. Lamotrigine was ineffective; seizures stopped with sodium valproate.
Conclusions: The self-induced seizures of Sunflower Syndrome are difficult to treat and are associated with physical, psychological and social impairments. Sodium valproate is the most effective medication which may be problematic in this predominantly female patient group.

Poster No. 035
What are the information needs of parents whose child is diagnosed with glutaric aciduria type 1 to help preserve neuro-developmental outcome?

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Objectives: To assess the information needs and support of parents at the time of diagnosis of GA1 in their child, and how to support them in preventing metabolic decompensation and preserving neuro-developmental function.
Methods: A focus group with five parents was conducted using a topic guide to direct the discussion, which was recorded and fully transcribed. Data were analysed using thematic analysis. Two researchers were involved in initial coding of data and key analytic decisions.
Results: Two main themes were identified. 'Understanding the condition' explored parent's needs to understand the scientific complexity of GA1 and to be aware of the 'worst case scenario' associated with loss of metabolic control, and brain injury. Parents reported clinicians did not give then enough information on the GA1, and were forced to use other information sources, sometimes seeking out scientific papers. Information on managing crises was insufficient, with parents not understanding what the doctor meant about commencing the emergency regime when their child was 'sick'. Parents reported living in terror of their child experiencing metabolic decompensation and permanent brain injury. 'Managing the condition' explained how parents coordinated and controlled the involvement of other carers and outlined parents' need to be active partners in medical management to feel in control. Parents wanted to know the results of regular biochemical tests for reassurance, but found they were not easily accessible. Parents could not leave their child in the care of another adult because they did not have sufficient knowledgeable about GA1 or were known to 'cheat' by offering the child food they should not have. The transition into school was a particular challenge.
Conclusions: The study highlights the importance of addressing parents' initial and ongoing informational needs so they can fulfil their role and protect their child from metabolic decompensation and permanent brain injury.

Poster No. 036
Normal transferrin isoelectric focusing in a child with COG4 related congenital disorder of glycosylation

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Objectives: Congenital disorders of glycosylation (CDG) are a large group of rare multisystem diseases caused by defective linkage of oligosaccharides to newly synthesised proteins or lipids. Several CDG subtypes are the result of mutations in subunits of the conserved oligomeric golgi (COG) complex. This includes COG4-CDG, an autosomal recessive disorder caused by pathogenic variants in the COG4 gene. In the two cases previously reported transferrin isoforms were abnormal, consistent with defective N-glycosylation.
Methods: We describe a 3-year-old female born to non-consanguineous parents. She presented with severe global developmental delay, dysmorphic features, postnatal progressive microcephaly, complex epilepsy, rhizomelia, spastic quadriplegia, and feeding problems from early infancy.
Results: MRI brain showed global cerebral atrophy, predominantly supratentorial, with relative cerebellar sparing. Trio exome sequencing and analysis identified compound heterozygous COG4 variants in the proband, a maternally inherited pathogenic splice site variant c.1061+1G>A and a paternally inherited likely pathogenic splice site variant c.1647+5G>A. Messenger RNA analysis showed that the c.1647+5G>A variant caused aberrant splicing, with skipping of exon 12 and the introduction of a premature stop codon in exon 13, likely to result in nonsense mediated decay. Analysis of transferrin isoforms was normal (by both isoelectric focussing and mass spectrometry). Since COG4-CDG also affects O-glycosylation apolipoprotein CIII (ApoCIII) isoelectric focussing was undertaken, however this too was normal.

Conclusions: Transferrin and ApoCIII isoelectric focusing are screening tests for N- and O-glycosylation defects. However, both have their limitations and some cases of CDG have normal transferrin or ApoCIII glycoforms escaping those screening tests. This is the first case of a patient with COG4-CDG with normal biochemical markers to be described. This case also demonstrates the diagnostic power of next generation sequencing for rare metabolic disorders, where the biochemical screening may be inconclusive.

Poster No. 037

Developmental delay in a young infant with non-classical combined malonic and methyl malonic aciduria (CMAMMA) caused by homozygous missense mutation in ACSF3 gene

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Introduction: AcylCoA synthetase family member 3 (ACSF3) activates malonylCoA and methymalonylCoA into their respective thioesters. ACSF3 deficiency causes non-classical CMAMMA, a rare inborn error of metabolism characterised by presence of methyl malonic acid in higher concentrations than malonic acid in urine. The reversal is seen with classic CMAMMA caused by malonylCoA decarboxylase deficiency (MCD).
Case report: 5-and-a-half-month old male infant second born to consanguineous South Asian parents presented with severe failure to thrive and recurrent vomiting. His older sibling who had failure to thrive and neuro-developmental delay died at 7 months without a genetic diagnosis. Initial blood tests revealed metabolic acidosis, pancytopenia and coagulopathy. Neuroimaging was unremarkable. Subsequent evaluation revealed normal levels of methionine, homocysteine and red cell folate. Significant methylmalonic aciduria with mild malonic aciduria without evidence of other abnormal metabolites (propionyl-CoA metabolites: hydroxypropionate, and methylcitrate or tiglylglycine) in urine suggested the diagnosis of non-classic CMAMMA, confirmed by homozygous missense variants in ACSF3 gene revealed by trio-exome sequencing. Neurodevelopmental assessment at 8 months revealed global developmental delay with general hypotonia; gross motor (4–6mo); fine motor (4–6mo); speech (5–6mo) and social (under 6mo), and without any regression. Carnitine was supplemented to avoid secondary depletion caused by the excretion of MMA. Parents were advised to avoid prolonged fasting and to provide emergency regimen (powdered carbohydrate drink mix) in the event of acute deterioration.
Conclusions: This report describes an unusual paediatric presentation of non-classic CMAMMA. Urine organic acids allows identification of increased MA and MMA excretion and highly suggestive of the diagnosis, thus avoiding additional investigations Determination of urinary MMA/MA ratio can help differentiating between classical and non-classical forms.

Poster No. 038

The clinical spectrum of paediatric patients with late onset Pompe disease

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Background: Late onset Pompe disease (acid maltase deficiency, glycogen storage disease type II) is a slowly progressive myopathy caused by the deficiency of α-glucosidase.
Objective: We are reporting the clinical phenotype, diagnoses and management in five children with late onset Pompe Disease.
Methods: We conducted retrospective case note analysis of the five Paediatric cases with confirmed diagnosis of the late onset Pompe disease, referred to the highly specialised metabolic service.
Results: Three of five patients (current age 14–22y) presented with delayed motor milestones in early childhood (mean age: 3.3y). One patient initially presented with episodes of thigh pain and high CK. In addition, when 10 years he re-presented with recurrent abdominal pain with high CK. The remaining one presented with muscle pain upon exercise with high CK. All apart from one had muscle weakness affecting limb girdle muscles and axial muscles. The remaining one presented with proximal muscle weakness by the age of 19 years. All patients remained ambulant, one developed scoliosis and two were on non-invasive ventilation. Cardiac involvement as ventricular dysfunction requiring targeted treatment was observed in one. Pathology showed vacuolated deposits in three patients and non-specific myopathic changes in one. Four are on enzyme replacement therapy (ERT) and tolerated well.
Conclusions: Late onset Pompe disease is a multisystem disease and should be considered in cases of isolated respiratory problems, lower back pain, rigid spine, and myopathy or exercise intolerance with elevated serum CK if these symptoms cannot be attributed to another disorder.

Poster No. 039

Delay in diagnosis and misdiagnosis of ataxia-telangiectasia: a systematic review

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Objective: To investigate the delay in diagnosis of ataxia telangiectasia.
Methods: Seventeen searches were carried out in each of 5 databases (Ovid SP (Medline), EMBASE, Web of Science,

PubMed, Scopus). The Cochrane Library was also searched. The search protocol is available. The inclusion criteria were: all dates, all languages, all ages, human participants and clinical relevance. The exclusion criteria were: no reference to ataxia-telangiectasia within the article, not an original article, animal studies, article not clinically relevant.
Results: Search returned 184 541 articles; 13 868 titles and abstracts were reviewed after removing 170 673 duplicates. Full text review includes 1106 articles of which 343 case series and 459 case reports were identified (12 518, exclusions; 244, articles not found or not accessible). Mean age of first sign or symptom of A-T in 563 cases reviewed to date was 31.4 months (range – 11d to 312mo). The mean age of diagnosis in 209 cases in which it has been reported was 81.4 months (range – 22d to 624mo). There was a mean time of 34.9 months from presentation to clinician, to diagnosis of A-T (range – 0 to 306mo, median 11mo) in the 71 cases in which this was reported. 20/563 (3.6%) cases had a documented alternative diagnosis prior to the diagnosis of A-T. 10/20 (50%) of these children were incorrectly diagnosed with cerebral palsy and 3/20 (15%) with hyper-IgM syndrome. The mean delay from incorrect diagnosis to a diagnosis of A-T was 87 months with the longest delay 306 months.
Conclusions: This study is the first comprehensive systematic review of scientific literature on ataxia-telangiectasia. We aim to describe the natural history of the condition and, along with results from the Natural History of A-T (N-HAT) study, systematically define, where possible, the conditions presentation, course, and prognosis.

Poster No. 040
Neurological presenting features of ataxia-telangiectasia: a systematic review

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Objective: To document the neurological presenting features of Ataxia-Telangiectasia (A-T).
Methods: Seventeen searches were carried out in each of 5 databases (Ovid SP (Medline), EMBASE, Web of Science, PubMed, Scopus). The Cochrane Library was also searched. The search protocol is available. The inclusion criteria were: all dates, all languages, all ages, human participants and clinical relevance. The exclusion criteria were: no reference to ataxia-telangiectasia within the article, not an original article, animal studies, article not clinically relevant.
Results: Search returned 184 541 articles; 13 868 titles and abstracts were reviewed after removing 170 673 duplicates. Full text review includes 1106 articles of which 343 case series and 459 case reports were identified (12 518, exclusions; 244, articles not found or not accessible; 304, other article types). 621 case series and case reports have been reviewed to date. 891 neurological presenting features have been reported in 751 cases. 603/751 (80%) people with A-T presented with gait ataxia or disturbance, and 13/751 (1.7%) with truncal ataxia. The most common presenting feature in cases without ataxia were developmental delay, or regression, and choreoathetoid movements. The second most common neurological presenting sign was dysarthria in 118/751 (15.7%) cases, and at least 2 of these had no associated ataxia. Dystonia was a presenting sign in 37/751 (4.9%) cases, including 3/37 (8.1%) with no associated ataxia. 64/751 (8.5%) initially presented with no neurological signs or symptoms.
Conclusions: This study is the first comprehensive systematic review of scientific literature on ataxia-telangiectasia. These results show that 91.5% of people with a diagnosis of A-T presented initially with at least one neurological sign or symptoms. This completed review will lead into the Natural History of A-T (N-HAT) study, a longitudinal, retrospective and cross-sectional study.

Poster No. 041
The role of serum oxysterol in the diagnosis of Niemann Pick C

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Introduction: Neimann Pick C is a neurovisceral disease that is caused by cellular cholesterol trafficking disruption. Historically, the diagnosis of Niemann Pick C was made using filipin staining and skin fibroblast cultures. Recently genetic testing of NPC1 an NPC2 genes are available. Mutations of either gene also affect cellular trafficking of cholesterol and detecting oxidative cholesterol metabolities can also be diagnostic of Nieman Pick C. Serum oxysterol can be used as a first line test with subsequent genetic confirmation and has a positive predictive value of >97%.
Methods: We present a case of an 11-year-old boy who was referred to genetics initially with absence of up gaze, severe restricted downward gaze, developmental delay, regression of skills and frequent falls. In the last 1 year his parents and school observed progressive deterioration of his symptoms with gelastic cataplexy, markedly decreased tone, increasing difficulty with memory loss and slurred speech. These symptoms are strongly suggestive of Niemann Pick C disease and oxysterols were requested which showed elevated oxysterol level of 128.7ng/mL (normal range 9.6–37). He was started on Miglustat. Genetics confirmed the diagnosis.
Results: Overall the child's parents report that since commencing the Miglustat he is more confident and they have recently seen him hop and skip which they haven't seen in quite a while.
Conclusions: Oxysterol is suitable biomarker for Neimann Pick C disease and can be used as first line with the genetic confirmation of gene NPC1 and NPC2 at later stage. As modifying treatment with Miglustat is available it is important to attempt diagnosing the condition as early as possible and oxysterol level can be used as screening test for Neimann Pick C when clinically suspected.

Poster No. 042
Biotinidase deficiency presenting with focal epilepsy in infancy

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Introduction: Biotinidase deficiency is a rare autosomal recessive inborn error of biotin metabolism. Biotinidase catalyses biocytin to biotin, a deficiency of which can present with neurological symptoms including hypotonia, seizures, feeding difficulties, lethargy, optic atrophy, and sensorineural deafness.
Case: A 9-week-old female presented with a 4-week history of seizures and developmental delay. Examination revealed generalised and axial hypotonia and delayed smile. She continued to have seizures despite initial treatments including levetiracetam and carbamazepine. MRI brain was normal and initial interictal EEG on Day 1 post admission revealed no significant abnormalities. Ambulatory EEG on Day 10 showed a focal onset epileptic seizure with sharp and slow wave activity originating predominantly from the left occipito-parietal region. Normal investigations included paired plasma and CSF glucose, lactate and culture, CSF neurotransmitters, microarray and epilepsy gene panel. On Day 11 post admission her biotinidase result was reported showing no activity. Biotin was commenced at 10mg once daily and her seizures abruptly stopped. She was discharged home on Day 14 and weaned off levetiracetam and carbamazepine. Her development was normal at 12-month follow-up. Genetic testing was declined by the family.
Discussion: Biotinidase deficiency can present from the neonatal period up to 10 years of age with a mean age of 3.5 months. In recent years our understanding of pathogenic changes in the biotinidase gene has increased through sequencing for novel mutation. This has important implications for families and consideration should be given to offering affected families genetic counselling. Treatment is available with oral biotin that rapidly improves symptoms, with seizures usually resolving within days and other symptoms showing improvement within weeks.

Poster No. 043
EEG to the rescue

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Objective: We present a previously well 16-year-old boy with a known m.3271T>C mutation experiencing 2 weeks of vomiting, lethargy and exercise intolerance.
Method: He was mildly dehydrated, fully consciousness but tachycardic and hypotensive. His pH was 7.28 with BE –17.3, HCO3 9.4 and lactate of 16.4. Electrolytes, FBC and inflammatory markers were normal. He was admitted to PICU for fluid management and sodium bicarbonate. Tachycardia persisted during the first 24 hours though he remained stable. He had a good urine output, was on non-invasive monitoring and an echocardiogram was normal. His gas lactate ranged from 14.1 to 16.8. The following day he deteriorated with Kussmaul respirations, tachypnoea, increased tachycardia and hypotension. Venous blood revealed a pH 7.14, pCO2 1.6 HCO3 11.3 BE –19 and lactate 18.5. He became unresponsive with refractory hypotension and multiorgan failure. Arterial blood showed a pH 6.8, pCO2 5.3 and a lactate >20 with indeterminable BE or HCO3. For over 24 hours he had a blood lactate level of >20. Rhabdomyolysis and acute kidney injury occurred with a CK of >200 000 requiring haemofiltration. Encephalopathy, with multiple white matter microhaemorrhages on MRI brain, and acute liver failure, with thrombocytopenia and coagulopathy, ensued. Multiple inotropes were required. The prognosis was very guarded. Off sedation he was unresponsive, apnoeic and areflexic however an EEG showed an alpha rhythm which prompted on-going heroic efforts. He required prolonged haemofiltration, ventilation and inotropes with 26 days intensive care.
Results: The patient made an astounding recovery. He required 1 month of neurorehabilitation and returned to his cognitive baseline, achieving A grades at GCSE 5 months later. Liver and renal dysfunction resolved.
Conclusions: This case demonstrates that mitochondrial metabolic crises in MELAS can be severe and result in profound acid-base derangements. Our patient was expected to not survive but uniquely did so without significant neurodisability.

Poster No. 044
Neuronal ceroid lipofuscinosis in children from Central Africa

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Objective: The effective and rapid diagnosis of neuronal ceroid lipofuscinoses (NCLs) has become more relevant with the advent of disease-modifying treatments. Some NCLs have a more stereotyped clinical presentation: we describe two cases in a non-consanguinous family, originally from the Democratic Republic of the Congo, with variant NCL.
Methods: Retrospective case series.
Results: The index case was initially diagnosed with a focal epilepsy: on review this child had myoclonic seizures in the context of a slow developmental decline, with mild spasticity. Ophthalmology was not diagnostically helpful, and a putative diagnosis of NCL was suggested by lymphocyte inclusions. Neither enzyme nor DNA analysis was available at that stage, although DNA was retained. A brother presented with nystagmus and visual inattention in 2017: examination showed myoclonic jerks with a bull's eye maculopathy and an abnormal peripheral retinal vascular leak. MRI imaging showed some element of cerebellar atrophy, which on review was also the case with his brother's scans. Some lymphocytes (20%) contained fingerprint bodies, suggestive of variant NCL. This was confirmed by DNA sequencing which was consistent with a diagnosis of MFSD8/CLN7-related NCL. The identical DNA alteration was also found in the index case.

Conclusions: NCL is not described in children from central Africa: the presentation, investigations and laboratory findings and evolution are consistent with that for other children with variant NCL.

Poster No. 045

Obesity screening of patients affected by Duchenne muscular dystrophy (DMD) in a tertiary paediatric neuromuscular centre and the effectiveness of metformin use in weight control in those with confirmed insulin resistance

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Objective: To assess whether patients affected by Duchenne Muscular Dystrophy (DMD) who are currently followed up in Alder Hey Hospital, UK are receiving obesity screening when clinically appropriate. To assess whether Metformin use in those who are insulin-resistant, has been effective in controlling weight.
Methods: Using the neurology department records, a list of patients with DMD currently under our services and those transitioned to adult services in the last 5 years, was generated. The patient record system, MediTech, was used to collect patients' demographics, latest weight/height value and BMI. For patients classified as overweight/obese, completion of obesity screening was assessed as well as initiation of appropriate treatment (Metformin). For patients on Metformin, the following parameters were collected: weight pre and post-steroids, age of start of excessive weight gain, confounding variables and medications, weight/height/BMI at initiation of Metformin and at 6-monthly intervals, side-effects, cessation of medication and reasoning.
Results: Sixteen out of 90 patients were found to be above the 98th weight centile. In 38 patients, weight was at 3 or more centiles above height. Using the non-DMD standardised BMI classification, 47 patients were identified as being overweight/obese. 16 patients received obesity screening; 7 were found to be insulin resistant. 4 of those were started on Metformin. 7 patients overall were started on Metformin. 2 of those exhibited overall weight loss. 3 patients were found to have gained weight and 1 patient showed weight increase up to 18 months post-Metformin initiation with subsequent weight loss.
Conclusions: There is a need for a validated and agreed BMI classification in DMD. Screening for insulin resistance in this patient group should be considered for implementation as standard practice, especially if patient is classified as overweight/obese. A larger-scale study would be required to assess the effectiveness of Metformin in this patient population.

Poster No. 046

A report on three cases of Niemann-Pick disease type B with an atypical phenotype marked by neurological involvement

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Objective: Niemann-Pick disease (NPD) is an autosomal recessive metabolic disorder with a prevalence of 0.4 to 0.6/100 000 worldwide, marked by varying degrees of lipid storage and foam cell infiltration in tissues, associated with hepatosplenomegaly, pulmonary insufficiency or central nervous system involvement. NPD type A and B are allelic disorders caused by mutations in the sphingomyelin phosphodiesterase-1 gene, SMPD1 (11p15.1-15.4), characterized by a primary deficiency of acid sphingomyelinase activity, resulting in an accumulation of sphingomyelin. In contrast to NPD-A, NPD-B is the milder, later-onset form, with no neurological involvement. In this paper, we report on three paediatric cases with NPD-B who present an atypical phenotype marked by neurological involvement.
Methods: The three patients were diagnosed at the age of 1 with hepatosplenomegaly. The first is a girl who presented psychomotor regression at the age of 3 and epileptic seizures at the age of 10. She died at the age of 15. The second is an 8 years old girl who presented growth retardation, kyphosis and neurodevelopment regression since the age of 6. The third is a 15 years old boy with a mild phenotype marked by developmental delay and an aggressive behaviour. Splenectomy was performed at the age of 8.
Results: Genetic testing was performed, and all patients presented mutations of the SMPD1 gene, confirming the diagnosis of Niemann-Pick type B. The c.1177T>G(p.Trp393Gly) mutation was common in all cases. In addition, heterozygous mutations c.573delT(p.Ser192Alafs*65) and del c.560_606del were found in the first and second case, respectively.
Conclusions: All cases present a complex phenotype, marked by psychomotor regression which is atypical for NPD type B. The severity of the disease seems to be correlated to the genetic mutation- the most severe phenotype was associated with c.573delT. Further work is necessary to more clearly delineate genotype-phenotype relationship in NPD.

Poster No. 047

Role of fluid management in the outcome of children with acute encephalitis syndrome

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Objective: Acute encephalitis syndrome (AES) is a group of symptoms and signs, which help diagnose encephalitis. Since

there is no definite treatment for most, role of fluids seems crucial. Therefore, the objective of our study was to describe the association of low admission weight and weight loss in the hospital (as clinical marker of dehydration) with outcome of patients of acute encephalitis syndrome.

To describe the association between changes in weight and blood lactate levels (at admission and discharge as indicators of hydration and acid base status) and outcome in children with acute encephalitis syndrome.

Methods: All children aged 1 month to 14 years with fever and altered sensorium and/or new onset seizures from September 2011 to September 2012 attending Kanti Children's Hospital, Kathmandu, Nepal were recruited. Weight-for-age (WFA) using *Z* score and serum lactate were assessed at admission and discharge. Total fluid input and output was monitored daily.

Results: Of the 92 patients, 62% had low admission WFA or lost weight-after-admission (LWAA) (group A) and 38% no low WFA or didn't LWAA (group B). There was 19 times risk of death and 7 times risk of bad outcome (death or sequelae) in group A compared to B. Bad outcome was significantly associated with less admission WFA, more fluid deficit, and trend for higher admission serum lactate. Death was significantly more in those with low WFA, more LWAA, longer illness, more 5% dextrose and 0.5 normal saline, higher sodium and higher urea at admission.

Conclusions: Optimum & appropriate fluids may be lifesaving treatment option in children with AES. A randomized control trial of different volume and types of fluids is recommended.

Poster No. 048
Validation of World Health Organisation definition of acute encephalitis syndrome with central nervous system infection in Nepali children

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Objective: World Health Organisation (WHO) defines acute encephalitis syndrome (AES) as a person of any age, at any time of year, with the acute onset of fever and a change in mental status and/or new onset of seizures in order to identify patients with possible acute encephalitis (AE). The objective was to compare and validate WHO definition of AES with the diagnosis of all central nervous system (CNS) infections, bacterial meningitis (BM), viral encephalitis (VE) and Japanese Encephalitis (JE).

Methods: We conducted a prospective cross-sectional study recruiting children aged between 1 month to 14 years attending Kanti Children's Hospital, Kathmandu, Nepal with altered sensorium and two of the following: fever, seizure, focal neurological deficit, CSF pleocytosis, electroencephalogram and computer tomography suggestive of encephalitis, over 1 year. In these patients, VE was if CSF cell count was <1000cells/mm^3 (lymphocyte predominance) and absence of non-viral pathogens in the CSF or blood. BM was CSF cell count >1000cells/mm^3 (polymorph predominance) and CSF protein >0.45g/L and CSF/plasma glucose <40%, and/or positive Gram stain and/or bacterial culture. JE was VE with ≥40units of anti JE-IgM in the CSF and/or serum. All CNS infections were defined as, suspected cases by treating clinician with or without fever with LP showing CSF cells >4/mm3.

Results: Out of 38, BM was found in 47%, JE 21% and other causes in 32%. Although WHO definition of AES was not significantly associated with all CNS infections (p=0.069), it was significantly associated with VE (p<0.001, sensitivity 74%, specificity 93%, PPV 94%, NPV 70%) and BM (p<0.001, sensitivity 30%, specificity 7%, PPV 33%, NPV 6%).

Conclusion: We validate WHO AES definition of BM and VE as a significantly useful screening tool for children with these diseases specially in resource poor settings, endemic areas and where confirmatory tests were not easily available.

Poster No. 049
Case series of Aicardi Goutieres syndrome (AGS) in our local population

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Objective: The aim of this case series is to raise awareness of this autosomal recessive encephalopathic syndrome that presents after birth in the multi-ethnic population in England. Although Aicardi Goutieres syndrome (AGS) is rare, its importance lies in the fact that that its presentation may be mistaken for other neurological conditions associated with congenital infections.

Results: All 6 of the patients were seen in our paediatric outpatient neurology clinic. The age of presentation ranged from the neonatal period to the first 20 weeks of life. All 6 patients were of Pakistani origin and 5 were from consanguineous marriages. They all had an uneventful antenatal period with normal birth weight and head circumference. The initial presentation seems to be of poor feeding and irritability. Further observations include truncal hypotonia, limb spasticity intermittent dystonic posturing coinciding with the onset of poor head growth and chilblains. 3 of our patients had abnormal movements with diffuse slow wave electroencephalogram activity. Nystagmus with visual inattention and poor visual acuity were a typical finding in all of them by the age of 3 months. The CT scans showed cerebral calcification in all of them and MRI suggested brain atrophy. The most striking abnormality was a raised level of CSF interferon-alpha (INF-α) in an absence of other infection or metabolic disorder. CSF INF α is a reliable diagnostic marker and can thus be used to differentiate patients with AGS from other conditions. Three of our patients had the same gene mutation, RNASEH2C.

Conclusions: AGS is a rare disorder, however in patients from consanguineous marriages that depicts microcephaly, poor tone and global developmental delay, diagnosis of AGS should be considered. As AGS is a progressive neurological condition, early support and prognosis can be provided for affected families.

Poster No. 050
Mild encephalopathy with reversible splenial lesions (MERS) in a child with primary Dengue virus infection

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Objective: We report the association of Mild Encephalopathy with a Reversible Splenial Lesion (MERS) with a primary Dengue virus infection. This case implies the existence of a wider spectrum of neurological involvement in Dengue virus infections.
Case description: A 12-year-old girl presented with acute confusion, dysarthria and bilateral limb weakness following a 4-day history of fever. Symptoms resolved after 2 hours; neurological examination was completely normal. She later experienced a second episode of slurred speech, dysphasia and right arm weakness which lasted an hour. A contiguous lesion involving the genu, body and splenium of the corpus callosum and bilateral posterior periventricular white matter was evident on the MRI brain scan, with restricted diffusion and T2-hyperintensity. Cerebrospinal fluid analysis showed no inflammation and polymerase chain reaction assay for respiratory viruses was negative. Her clinical and radiological features were consistent with Mild Encephalopathy with a Reversible Splenial Lesion (MERS). On day 2 of admission, she developed a generalised maculopapular rash with leukopenia (white blood cell count 1.81×109/L) and thrombocytopenia (platelets 135×109/L). Serology (IgM/IgG) for Dengue virus was negative and a positive Dengue NS1 Antigen was thus indicative of a primary dengue virus infection. She was given fluid rehydration and advised bedrest. At discharge (day 6 admission) she was well with no sequelae.
Conclusions: MERS is a mild form of virus associated encephalopathy (VAE), which are a spectrum of clinico-radiological syndromes associated with common childhood viral infections. The clinical and neurological symptoms in our patient occurred early in the course of illness (typical to VAE) as opposed to after or late in the illness as is typical for postinfectious encephalopathy syndromes associated with dengue virus infections (e.g., acute disseminated encephalomyelitis).

Poster No. 051
Shouldering the burden of sepsis

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Aim: We report a case of a 15-year-old boy who presented with right brachial plexus neuritis secondary to meningococcal group B sepsis. Brachial plexus neuritis or Neuralgic Amyotrophy (also known as Parsonage -Turner syndrome) is a rare disorder affecting the brachial plexus. It can be caused by various infectious agents and is characterized by acute onset of intense pain in the shoulder and arm followed by weakness, sensory loss and atrophy.
Methods: A 15-year-old boy, previously fit and well presented to the Emergency Department with an acute onset of excruciating pain in his right shoulder, radiating down his arm and hand with associated paresthesia. Few hours later, he developed an evolving non-blanching purpuric rash to the chest, back, shoulder and right arm. He gradually developed weakness in the right arm and sensory loss over the ulnar aspect of the right hand. He then began to complain of headache, photophobia with subsequent vomiting. He was treated for meningococcal sepsis with intravenous ceftriaxone and received three fluid boluses for hypotensive shock with vitamin K correction for his associated coagulopathy. He received analgesia for right shoulder pain.
Results: Blood cultures and blood PCR confirmed Neisseria meningitidis group B type, NT subtype. MRI of the shoulder showed inflammation consistent with brachial plexus neuritis with motor impairment affecting the right side C4 to T1 myotomes and sensory impairment involving the right C6 dermatome. The patient was treated with oral prednisone and gabapentin whilst receiving neurorehabilitation from physiotherapy and occupational therapy. He made a very pleasing recovery after few months and currently has no motor or sensory deficit of his right shoulder and arm.
Conclusion: Brachial plexus neuritis should be considered in the differential when a child presents with sudden onset pain and weakness of the shoulder and arm. In review of literature, brachial plexus neuritis associated with meningococcal infection has not been described previously. To the best of our knowledge, this is the first reported case of its kind.

Poster No. 052
Paediatric primary progressive multiple sclerosis: fact or fiction?

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Introduction: Previous cohort studies on paediatric multiple sclerosis (MS) have reported very low frequencies for a primary progressive MS course (PPMS) ranging from 0 to 7%. An age-dependent increase in the rate of primary-progressive courses has been well described in the adult MS population.
Objectives and Methods: We describe five patients presenting prior to the age of 18 years and fulfilling the 2017 McDonald Criteria for PPMS. Patients were identified from the National Hospital for Neurology and Neurosurgery (NHNN) and the UK Childhood Inflammatory Demyelination (UK-CID) network.
Results: Patients presented at a median age of 15 years (range: 11–17y), with at least 1-year history of progressive deterioration of their balance (n=2) or progressive worsening of lower limb function (n=3). Over time, all patients developed lower limb spasticity, three patients developed cognitive difficulties, three had visual problems, three had bladder involvement.

Median EDSS at 2 years was 5 (range: 4 to 7). Cerebrospinal fluid (CSF) oligoclonal bands were detected in all 4 patients tested. Dissemination in space on first MRI was seen in all patients with peri-ventricular (n=4), cortical juxtacoritcal (n=2), infratentorial and spinal cord (n=4) lesions. All patients showed new lesions on repeat MRI imaging. Contrast enhancement was present in 3 out of 4 (75%) during the disease course. Three patients had genetic investigations to exclude other mimics. A trial of IV methylprednisolone was unsuccessful in 3 patients. All patients were on symptomatic treatment for spasticity and pain, including oral/intra-thecal baclofen, gabapentin and sativex.
Conclusions: Given the rarity of primary progressive course in paediatric MS, presentation with progressive neurological symptoms and signs in young people should prompt evaluation for genetic causes. Nevertheless, our five patients presented with clinical, MRI and immunological features consistent with a diagnosis of primary progressive multiple sclerosis.

Poster No. 053
Factors predictive of disease course and outcome in NMDAR-antibody encephalitis: a systematic literature review

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Objective: Clinical course in NMDAR-antibody encephalitis is variable and difficult to predict. We aimed to identify clinical features in the presenting disease episode associated with worse functional outcome and/or relapsing disease course.
Methods: Systematic review of the literature was conducted to identify published cases with individually reported data. Clinical and treatment characteristics at first episode, outcome at ≥12 months, and monophasic vs. relapsing disease course were recorded.
Results: 1651 cases were identified from 693 articles (73% female; 48% ≤18 years old at onset). 91% received immunotherapy at first episode: corticosteroids in 81%, IVIG in 66% and therapeutic apheresis in 33%. Second-line immunotherapies were used in 32% at first episode, most frequently rituximab (17%), cyclophosphamide (5.1%), or both (7.2%); emerging second-line treatments (intravenous/intrathecal methotrexate, subcutaneous/intravenous bortezomib, intravenous tocilizumab) were used in 1.8%. Life-threatening adverse events or death related to immunotherapy occurred in 1.9%. In a univariate analysis of 682 cases with ≥12 months follow-up data, poor final outcome (defined as modified Rankin Scale [mRS] score 3–6) occurred in 30% and was associated with very young or elderly age at onset, movement disorder, decreased consciousness, autonomic dysfunction, mechanical ventilation, higher mRS score in the acute phase, longer hospital stay, extreme delta brush on EEG, abnormal MRI, CSF pleocytosis and elevated CSF protein (all p<0.05). A subset of 198 cases followed up for ≥36 months were analysed to identify associations with relapsing course, which occurred in 29%. In univariate analysis, factors protective against relapse were <30 days delay in first-line immune therapy, therapeutic apheresis, IVIG, Rituximab and other second-line treatments at first episode (all p<0.05).
Conclusions: Worse functional outcome of NMDAR-antibody encephalitis is associated with very young or elderly age at onset and worse disease severity in the acute phase. Relapsing disease course is associated with delayed or insufficient early immunotherapy.

Poster No. 054
Is it 'CLIPPERS'? The expanding spectrum of paediatric demyelination; three cases of familial hemophagocytic lymphohistiocytosis (fHLH)

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Objective: We describe three children with familial Hemophagocytic Lymphohistiocytosis (fHLH), who presented with an atypical chronic demyelinating illness. An initial working diagnosis of 'CLIPPERS' (Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids) was made in two cases.
Methods: Retrospective case series.
Results: Case 1: An 11-year-old girl presented with diplopia and squint with evolving ataxia. MRI showed multiple enhancing white matter lesions in the pons, medulla and cerebellum raising the possibility of 'CLIPPERS'. Her symptoms and neuroimaging responded only partially to treatment with IVIG and steroids. Genetic testing revealed a compound heterozygote mutation in the RAB27A gene consistent with Griscelli Syndrome type 2 with fHLH. Case 2: A 5-year-old boy had nocturnal headaches with a squint evolving over time. MRI showed demyelination and swelling predominantly in the cerebellum. Significant radiological resolution with steroids was followed by recurrence of demyelination on weaning steroids. A brain biopsy lesion was consistent with 'CLIPPERS'. Genetic testing revealed a heterozygote variant in the STXBP2 consistent with fHLH V. Case 3: A 9-year-old girl had a 7-month of intermittent fevers, deranged LFTs and recurrent bilateral optic neuritis responsive to steroids/IVIG. MRI brain showed multiple areas of demyelination largely in the subcortical white matter. Oligoclonal bands were positive in the CSF. She developed a pleural effusion, high ferritin, deranged coagulation, lymphadenopathy and a rash found to be a cutaneous T-cell lymphoma. Genetic testing revealed a homozygous mutation in the UNC13 gene consistent with fHLH 3. All three children are awaiting stem cell transplantation.
Conclusions: fHLH can present with an isolated atypical demyelinating illness or with neuroimaging suggestive of

'CLIPPERS'. There may be no signs of systemic inflammation. We propose that all children with atypical recurrent CNS inflammation and presentations consistent with 'CLIPPERS' undergo genetic panel testing for fHLH and Natural Killer cell functional testing.

Poster No. 055

Myelin oligodendrocyte protein antibody (MOG-Ab) related seizures and epilepsy in UK paediatric patients

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Objective: The most common paediatric presentation of MOG-Ab disease is with acute disseminated encephalomyelitis (ADEM), or optic neuritis (ON). With increasing recognition of the association of MOG-Abs with seizures in children, we present a case series of affected children.

Methods: Retrospective anonymised case note review of affected children presenting between 2005- 2019, from 5 UK paediatric neurology centres. Patients were followed up for median of 6 years (range 0.5–16).

Results: 15 cases (7 female) of MOG-Ab-positive epilepsy patients were identified; median age at first presentation was 6 (range 2–14y). The most common preceding MOG-Ab disease was multiphasic ADEM (MDEM 6; ADEM 3; ADEM-ON 2; ADEM and transverse myelitis 1; NMOSD 2; ON 1). Median time to recurrent seizure onset was 3 months (range 0–60). Focal epilepsy/seizures were most common (12/15). EEG abnormalities were found in 14/15 patients, all demonstrated slowing/encephalopathy which was generalised or focal; epileptiform discharges were reported in 3 patients. Brain MRI was abnormal in all patients (8 with multifocal hazy/poorly marginated lesions involving grey and white matter; 4 leukodystrophy-like pattern, 2 cortical encephalitis and 1 reported with subtle changes in brainstem). 8 patients received immunotherapy, all required at least 1 anti-epileptic drug (AED) and 8 children continue to have on-going breakthrough seizures. Median MRS (Modified Rankin Scale) at last follow-up was 1 (range 0–3), indicating no significant disabilities despite symptoms in clinical examination, age appropriate behaviour and development.

Conclusions: Focal epilepsy is more common and more likely to follow an MDEM presentation in children with MOG-Abs. With the relapsing nature of MOG-Ab disease there is a high risk of long-term cognitive impairment. Further preclinical studies are urgently required to determine whether this epilepsy is due to ongoing inflammation or as a result of the MRI changes commonly seen. This will help inform future management decisions regarding immunotherapy.

Poster No. 056

Maternal mid-gestation cytokine dysregulation in mothers of children with autism spectrum disorder

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Autism spectrum disorder (ASD) is a developmental disorder characterised by a spectrum of deficits in social interactions/communication combined with stereotypical, repetitive behaviours. Recent evidence suggests maternal immune activation (MIA) during pregnancy may predispose offspring to ASD. The aim of this study was to examine the mid-gestation cytokine profile in mothers of children with a subsequent ASD diagnosis. Maternal-child dyads were recruited to a prospective population-based pregnancy study; the SCOPE study, New Zealand. Children with confirmed diagnosis of ASD at 6 years were enrolled in the nested cohort, along with matched neurotypical controls. Cytokine concentrations (pg/mL; mean [SEM]) were examined in maternal serum samples taken at 15 and 20 weeks gestation using Mesoscale Discovery proinflammatory, cytokine and chemokine assays. Of 2032 mothers recruited to the SCOPE-NZ study, 16 children completed follow-up and had reported ASD at 6 years. These were analysed alongside 16 neurotypical matched controls. Downregulation of IL-17A occurred at 20 weeks gestation in cases when compared to controls (mean [SEM]). 2-way ANOVA revealed a relationship between IL-17A concentration and weeks' gestation $F(1,49)=4.183$; $p=0.0462$, and also IL-17A concentration and ASD status F91,49)=7.801; $p=0.0074$. Posthoc uncorrected Fisher's LSD revealed a significant difference between cases (–0.3846 [0.1426]) and controls (–0.1207 [0.05068]) at 20 weeks gestation $p=0.0160$. IFNγ is also downregulated at 20 weeks gestation in cases when compared to controls. 2-way ANOVA revealed a relationship between IFNy concentration and weeks gestation $F(1,53)=5.692$; $p=0.0206$. Posthoc Uncorrected Fisher's LSD revealed a significant difference between cases (0.347 [0.0215]) and controls (0.4345 [0.1685]) at 20 weeks gestation $p=0.0476$. We have shown altered cytokine expression at 20 weeks gestation in mothers of children who progress to develop ASD. This adds to the growing body of evidence that maternal immune regulation may play a role in foetal neurodevelopment.

Poster No. 057

Getting to the heart of white matter

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Objective: Acute Disseminated Encephalomyelitis (ADEM) is an immune mediated inflammatory CNS disorder, predominantly affecting white matter, with a wide differential (1). Here we describe a rare mimic of ADEM that is essential to consider in order to avoid a catastrophic outcome.
Case history: A 12-year old girl presented with a 2 day history of confusion, dysarthria, ataxia and left-sided squint, preceded by 2 weeks of general malaise and headache. Examination confirmed encephalopathy and a left third cranial nerve palsy. MRI brain was suggestive of ADEM and MRI spine was normal. A recommended work up for ADEM was performed. Rapid resolution of her symptoms occurred following intravenous methylprednisolone for 3 days. 2 years later she presented with acute left lower limb ischaemia and underwent emergency embolectomy of a popliteal arterial obstruction, with myxomatous material identified. Preoperative echocardiogram confirmed a large atrial mass which was surgically removed. Pathology confirmed an atrial myxoma (AM). Retrospective review of her initial MRI images concluded that embolic phenomena from the AM was the most likely explanation of her first presentation.
Conclusions: AM is a very rare primary cardiac tumour and left sided AM can embolise to the cerebrovascular system. Early identification of AM is important as, untreated, it can cause multiple embolic events and sudden cardiac death. 12% of adults with AM present with neurological symptoms and this can mimic multiple sclerosis. AM presenting with acute neurological symptoms masquerading as ADEM in paediatrics has not been previously reported. Careful follow up is essential as late neurological complications (including cerebral arterial aneurysms) are recognised. This case highlights that ADEM is a diagnosis of exclusion and that mimics for acute focal neurology with encephalopathy and T2 hyperintensities on MRI require careful consideration, including embolic phenomena. Clinical examination alone does not exclude AM and consideration of echocardiography is recommended.

Poster No. 058

A case of a boy with Balo's concentric sclerosis

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We describe an 8 year old boy with a rare demyelinating disorder: Balo's concentric sclerosis. A routine optician review raised concerns about papilloedema in an asymptomatic child. A CT brain identified a well-demarcated high-density lesion in the left posterior frontal lobe with surrounding oedema. MRI brain with contrast identified the lesion had central rim enhancement and slight diffusion restriction. Alternating layers of high and low signal intensity gave it an 'onion bulb' appearance. The differential included Balo's concentric sclerosis, a single demyelinating lesion, or a tumour. Routine blood tests were unremarkable. CSF oligoclonal bands were normal as were other CSF indices. Markers of immunology, including ANA, ANCA, anti-MOG, anticardiolipin, and aquaporin 4 antibodies were all negative, with normal complement levels. ESR was mildly elevated when taken during an episode of acute tonsillitis. Imaging 3 months later demonstrated an increase in the size of the lesion. A biopsy revealed inflammatory demyelinating pathology mediated by a perivascular and parenchymal T-and B-lymphocyte infiltrate and macrophage activity with associated demyelination lacking a perivenular distribution. There was no evidence of neoplasia, vasculitis, granulomas, or viral infection (including negative PCR testing). No treatment with corticosteroids was given, and the child remained asymptomatic. Imaging, at 9 months from presentation, revealed the lesion had substantially reduced in size. There was still a rim of enhancement. As with all single demyelinating lesions, it is difficult to predict the clinical course. We opted to adopt a 'wait and see policy' and offer surveillance imaging and clinical review. Balo's concentric sclerosis is a rare demyelinating disease, characterized by concentric lamella of alternating demyelinated and partially myelinated tissues. MRI shows one or more concentrically mulitlayered ring-like lesions, usually in the cerebral white matter. Most case reports describe cases predominantly in young adults, with few reports of cases in children.

Poster No. 059

Evolving cognitive dysfunction in children with neurologically stable opsoclonus-myoclonus syndrome

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Objective: Cognitive and acquired neurodevelopmental deficits have been reported in children with opsoclonus-myoclonus syndrome (OMS) and are associated with more severe and relapsing disease course. However, there is a paucity of data regarding cognitive dysfunction in children with stable neurological disease. We report on serial cognitive assessments of 4 children with OMS demonstrating evolving cognitive dysfunction with milder disease course.
Methods: Retrospective analysis of clinical features at presentation, investigations, treatments, clinical course including relapses and neuropsychological testing.
Results: Four children (M:F 1:1) diagnosed with OMS between 17 and 35 months were followed up for 4 to 10 years. Neuroblastoma was identified in one child. OMS severity scores

ranged between 8 to 12/15 at presentation. Patients underwent immunotherapy in accordance with European OMS protocol. All patients were in remission by 7 months (range 4–13mo), with treatment maintained for 1 year. One child remained relapse free whilst 3 other children had one clinical relapse which was immunotherapy responsive again. In all cases, progressive cognitive dysfunction was reported despite being in remission and stable off treatment for 20 months (range of 12–31mo; 3 OMS score 0/15 and one 2/15). Sequential neuropsychological testing scores showed mean declines in FSIQ of 16 (13–19), VIQ of 24 (20–27) and PIQ of 17 (–2 to 30) between time of OMS remission/stable disease and longer term follow-up time point (4–10y).
Conclusions: Our cases demonstrate progressive cognitive dysfunction occurring in children with OMS who have a milder disease and long after completion of treatment. Children continued to develop but with a widening gap in comparison with peers. Damage to cerebellar-cortical circuits at onset of the disease that becomes more apparent with time or indeed persistent ongoing low grade inflammation may explain this deterioration.

Poster No. 060
Three cases of enterovirus D68 associated acute flaccid paralysis in a tertiary paediatric neurology centre

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Introduction: The past decade has seen increasing cases of acute flaccid paralysis (AFP) associated with Enterovirus D68 (EVD68) infection. It presents in clusters approximately every 2 years. We report three cases of AFP due to EVD68 that presented in November-December 2018.
Cases: Two patients developed AFP following a viral upper respiratory tract infection and one developed lower limb hypotonia and weakness during an inpatient admission with refractory epilepsy. Two required admission to the paediatric intensive care unit for respiratory compromise and required tracheostomy ventilation. MRI showed acute flaccid myelitis (AFM) consistent with EVD68 in 2/3 cases, consisting of central cord T2 hyperintensity in the cervical region over multiple segments with subsequent enhancement of the thalamus and cauda equina on follow-up imaging in one patient; and ventral surface enhancement of the conus and cauda equina in another. MRI in the third patient was normal. Electromyography and nerve conduction studies were normal in two patients but revealed a severe generalised motor axonal poly-neuronopathy in the third. Two patients received intravenous immunoglobulin, corticosteroids or plasma exchange therapy and showed slow motor improvement in a distal to proximal pattern. The one patient without MRI changes had received long-term oral corticosteroids but received no additional treatment and returned to baseline neurological function within 4 weeks.
Discussion: Our cases demonstrate the range and clinical course of peripheral neurological presentations secondary to EVD68 infection. We highlight the importance of sending repeat samples from multiple sites when the diagnosis is suspected, given that initial samples tested negative, and of sending samples to a national surveillance laboratory for confirmatory testing. Ongoing national and multinational surveillance studies will hopefully continue to advance our understanding and treatment of this disease.

Poster No. 061
NMDA receptor encephalitis a potential complication of biologic therapy for juvenile idiopathic arthritis?

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A 12-year-old girl presented with headaches, confusion and agitation, followed by seizures. She had presented at 20 months with polyarticular arthritis and was managed over subsequent years on methotrexate alone (2y) with added etanercept (anti-TNF alpha, 5y), tocilizumab (anti IL-6, 2y) and abatacept (CD 80/86 T-cell modifier, 3y prior to presentation). Flares of disease following a period of control necessitated the changes in monoclonal antibody therapy. At this presentation she was managed on methotrexate, abatacept and 5mg prednisolone for polyarticular rheumatoid factor negative juvenile idiopathic arthritis (JIA). At presentation the patient was agitated, non-verbal and had one generalised seizure. Examination demonstrated acute confusion, with increased tone, brisk reflexes and bilateral clonus in her lower limbs. IV ceftriaxone, acyclovir and clarithromycin were commenced. Full blood count, liver function tests and inflammatory markers were unremarkable. Infective serology was non-contributory. CSF was unreactive with normal protein and JC virus PCR negative. MRI brain 5 days after presentation showed increased T2 and FLAIR signal intensity in the white matter of the right parietal lobe, in-keeping with an inflammatory process. EEG showed diffuse slowing with delta brush. She commenced IV methylprednisolone, followed by prednisolone. She continued to deteriorate and underwent plasmapheresis for treatment of presumed NMDA receptor encephalitis, subsequently confirmed by anti-NMDA receptor antibodies in serum and CSF. She was commenced on Rituximab (B-cell depletion, anti-CD 20), and continued to undergo plasmapheresis over the course of 4 weeks. She gradually improved and was discharged home after a 10-week inpatient stay. Several adult and two paediatric cases of NMDA receptor encephalitis are reported in patients on biologic therapy for autoimmune disease. Autoimmune diseases are more common in those already affected by one autoimmune condition. It is unclear what contribution an autoimmune history or immunomodulation made on the development of this condition.

Poster No. 062

A 10-year single centre review of transverse myelitis-plus

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Introduction: The incidence of Acute Flaccid Myelitis (AFM) associated with enterovirus infection occurring in biennial clusters since 2012 has been reported in the US (BMJ 2018, 18; 363:k5246) and recently in Europe. Previously, cases with transverse myelitis (TM) with anterior-horn cell or peripheral nerve involvement have been collectively termed TM-plus (Neurology 2016; 87;S46-S52). We aimed to identify cases of TM-plus from a retrospective cohort of children to identify potential cases of 'undiagnosed' AFM, and to evaluate the clinical and radiological features alongside long-term outcome.
Methods: Consecutive cases of children (<16y of age) who presented to a large paediatric neurosciences centre from 2009 to 2016 fulfilling the Transverse Myelitis Consortium Working Group criteria modified for the paediatric population (*Neurology* 2015; 84:341–349) were retrospectively evaluated for additional features of anterior horn-cell involvement (fulfilling criteria for AFM (*Current Treat Options Neurol* (2017) 19: 48)) or peripheral nervous involvement; and were collectively evaluated with the contemporary TM-plus cohort (2016–2018).
Results: 25 cases of TM were identified, 7 of which were excluded from further analysis; MS (n=6), ADEM (n=1). 8 cases of TM-plus were identified, 4 before 2016 and 4 after, all associated with a viral prodrome. Flaccidity (n=8) and asymmetry (n=6) was noted at presentation, with corresponding nerve conduction studies revealing a motor axonopathy with sensory sparing (n=6) and anterior horn cell involvement confirmed in 3 cases. All cases with anterior horn cell involvement had poor outcomes while both cases with good outcomes had peripheral involvement and normal MRI brains.
Conclusions: TM-plus was detected in our cohort from 2009 to 2016 with biennial clusters noted in 2016 and 2018. The clinical presentation, investigations and long-term outcomes appear consistent in both groups.

Poster No. 063

Acute necrotising encephalopathy is more severe when associated with influenza

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Background and objective: Acute Necrotising Encephalopathy (ANE) is a rare but potentially life-threatening condition associated with viral infections. A familial and recurrent form (ANE1) has been identified by mutations in the nuclear pore Ran Binding Protein (RANBP2). We report the morbidity and mortality when associated with Influenza infection.
Methods: We performed a review of paediatric ANE cases from 1999 to 2019 evaluating the clinical, biochemical, microbiological and neuroimaging appearances as well as outcomes.
Results: The cohort comprised 6 children (2 boys), age ranging from 8 months to 3 years 9 months (<2y n=5), of which 4 had a confirmed genetic diagnosis and 2 were RANBP2 negative. There were 13 episodes of encephalopathy, with recurrences in 3 cases (2 ANE1). 10 of these episodes had infectious aetiology identified: coronavirus n=2, parainfluenza n=1, adenovirus n=2, H influenzae n=1, influenza (H1N1 n=3, H3N2 n=1). Clinical features of fever and encephalopathy were consistent (100%), and seizures and sixth nerve palsies prominent (50% each). CSF revealed absent pleocytosis, normal-elevated protein and negative virology. Symmetric involvement of the thalami bilaterally was present in all cases, and all ANE1 cases were associated with haemorrhage and external capsule/claustrum involvement (100% specific and sensitive). The outcome following influenza infection was striking, death n=1, vegetative n=2, 4 limb motor and movement disorder n=1. 2 of these cases had previous episodes of encephalopathy with non-influenza infection and did have recovery, albeit with moderate to severe disability. All 3 cases were never immunised against Influenza infection and suffered grave outcomes.
Conclusions: Influenza infection in ANE has the poorest outcome therefore vaccination should be a mandatory consideration for the known cases of ANE.

Poster No. 064

Acute flaccid paralysis: a case series from the east of England

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Introduction: Acute Flaccid Paralysis (AFP) is characterized by a rapid onset of limb weakness. We describe six cases of AFP in children aged 9 months to 3 years of age who presented to a tertiary Paediatric Neurology service in the East of England over a 5-year period from November 2013–November 2018. Retrospective analysis of the six cases was performed, reviewing their clinical course and management, as well as their radiological, electrophysiology and laboratory results.
Results: Case 1, a 9-month-old boy, presented in November 2013 with a viral URTI requiring escalation of care to PICU due to a significant respiratory compromise. Only on subsequent recovery was the child found to have a unilateral upper limb flaccid paralysis. This child was positive for enterovirus serotype D68. Cases 2 and 3 in our series presented in 2016 with acute weakness of the lower limbs with an MRI brain and spine showing enhancement of the lumbar spinal roots. Both have made a good recovery. Enterovirus was not

detected in either case. The final three children in our series presented in Autumn 2018 with weakness of a unilateral upper limb following a viral URTI, with all three being positive for enterovirus. Unfortunately, they have shown minimal recovery of motor function of the affected upper limb. One child, a 3-year-old girl, showed a more severe clinical course involving a prolonged period of intensive care and a tracheostomy for long-term ventilation. She has undergone neurorehabilitation and an upper right arm nerve transfer.
Conclusions: In our case series, four patients presented with an acute viral URTI associated with an upper extremity weakness, and subsequently all four were positive for enterovirus. Clusters of acute limb weakness in paediatric patients have been linked to outbreaks of non-polio enteroviruses, termed acute flaccid myelitis (AFM).

Poster No. 065
Recurrent anti-MOG demyelinating disease, is stopping steroids worth the risk?

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Objective: To present an interesting case of recurrent anti-MOG demyelinating disease and provoke discussion regarding possible immunomodulatory therapy.
Methods: A 14 year old girl presented, initially at 5 years of age, with headache and vomiting. She was initially treated as atypical tuberculosis meningitis based on CSF cell counts, but later developed a 6th nerve palsy and was diagnosed with optic neuritis. Anti-MOG antibodies were positive and they were commenced on IV methylprednisolone. She clinically improved and was discharged on weaning oral prednisolone, antibodies were negative following treatment.
Results: A few months later she had her first relapse, with an acute decline in visual acuity. An MRI showed new lesions in her optic chiasm and both optic nerves with associated bilaterally reduced visual evoked potentials. She was again treated with IV methylprednisolone, with rapid improvement, followed by a switch to weaning oral prednisolone. Anti-MOG antibodies were negative following treatment. She was symptom free for 7 years until her second relapse, when she presented with facial palsy, swallowing difficulties and slurred speech. MRI showed brainstem and periventricular white matter demyelination, with positive anti-MOG antibodies. She was again treated with IV methylprednisolone, followed by oral prednisolone, but was maintained on low dose prednisolone as her anti-MOG antibodies remained weakly positive despite being symptom free. These were stopped at patient request due to low mood and abdominal pain in February 2019, with no recurrence of symptoms as yet. Repeat MOG antibodies have been sent and are awaited.
Conclusions: This case shows an interesting relapsing/remitting pattern of Anti-MOG demyelinating disease, which appears to be very steroid responsive, however on her second relapse her anti-MOG antibodies remained weakly positive despite steroid therapy. Discussion is welcomed on whether prophylactic immune modulation therapy should be considered with this child, such as azathioprine, mycophenolate mofetil or rituximab.

Poster No. 066
Acute presentations of multiphasic acute disseminated encephalomyelitis: a case series

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Objective: To highlight the utility of early MR imaging in children presenting with acute severe encephalopathy and to consider whether there might be a subgroup of children with myelin oligodendrocyte glycoprotein antibody (MOG-Ab)-associated demyelination who might be candidates for early intense immunomodulation.
Methods: We report two cases with MOG-Ab-associated acute demyelination who relapsed with new neurological symptoms after initial steroid therapy had been discontinued.
Results: Two toddlers were initially admitted to intensive care with acute encephalopathy and acute symptomatic seizures. Both had an initial CT head during PICU admission; one was reported normal; the other was suggestive of diffuse cerebral oedema. Both children improved with supportive care only and were discharged home within a week. Both children presented again over the following 2 to 4 weeks with new neurological symptoms but without encephalopathy. MR imaging demonstrated demyelination and they were treated with steroids. Both children relapsed as steroids were being weaned and/or stopped. Repeat MR imaging at this stage demonstrated new enhancing lesions. It was subsequently found that both children were MOG-Ab positive.
Conclusions: Reliance on cranial CT imaging in the context of a young child with acute encephalopathy and seizures can be misleading.

Prediction of the severity of MOG-Ab-associated demyelinating syndrome at onset is challenging. MR imaging in the acute phase with early follow up imaging may identify this subgroup.

Poster No. 067
Tolosa-Hunt syndrome; a rare cause of painful ophthalmoplegia in childhood

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Case: HB is a 7 year old boy who presented with sudden onset diplopia and painful ophthalmoplegia, following a 12 day history of frontal headache. On examination, he had a left VIth nerve palsy, partial left IIIrd nerve palsy and normal right eye movements. The remainder of his neurological and general systems examination was normal. His initial CT head scan and pre-contrast MRI of the brain were normal. He was discharged from the local hospital following normal blood tests and imaging.
Clinical course: Nine days later, his symptoms worsened including severe vomiting, worsening frontal headache and photophobia. He was treated for a possible underlying infective

cause with Ceftriaxone and Acyclovir. Given the broad underlying differential diagnoses, HB had extensive infectious and immunological blood workup which was unremarkable. A repeat MRI brain scan with contrast revealed a lesion in the left cavernous sinus, possibly of vascular origin. Differentials included cerebrovascular venous sinus thrombosis, tumour and inflammatory causes such as TB, sarcoid and zoonoses. HB continued to be conservatively managed and completed his course of Ceftriaxone and Acyclovir. Repeat MRI imaging 2 months later showed some resolution of the lesion and a diagnosis of Tolosa-Hunt syndrome was provisionally made. HB's symptoms continued to improve and further repeat MRI scan 6 months later showed ongoing resolution of the lesion.
Discussion: According to the ICHD-3 beta classification of Tolosa-Hunt syndrome, HB fulfilled the diagnostic criteria given his presentation of unilateral headache, granulomatous inflammation of the cavernous sinus on MRI, palsies of ipsilateral IIIrd, IVth and VIth cranial nerves. Steroid use has been reported to be beneficial although more evidence is required in the paediatric population, refractory cases may respond to Azathioprine and Methotrexate.

Poster No. 068
Cerebral folate deficiency associated with internuclear ophthalmoplegia

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Objective: We present a case of internuclear ophthalmoplegia unresponsive to steroid treatment which clinically improved with folinic acid supplementation.
Method: A retrospective chart review.
Results: Our patient presented with acute internuclear ophthalmoplegia, ataxia and bilateral ptosis. She had a background of hypoplasia of the corpus callosum and optic atrophy with visual impairment, learning difficulties and ASD.

MRI brain demonstrated symmetrical high signal intensity in the region of the medial longitudinal fasciculus and periaqueductal grey matter. She was investigated to exclude an inflammatory cause and was treated with high dose steroids. Follow up MRI did not show any improvement post steroids and there was no clinical improvement. Subsequent CSF investigations showed a low level of 5- methyltetrahydrofolate of 35nmol/L (normal range 72–172nmol/L). She was commenced on folinic acid 15mg once daily and her symptoms improved. On follow up her eye movements had significantly improved as had her ptosis. Follow up MRI brain showed partial resolution of the areas of abnormal signal in the periaqueductal grey matter.
Conclusion: Internuclear ophthalmoplegia is a sign usually associated with an inflammatory or demyelinating cause. Our case did not respond to steroid treatment but has associated low levels of 5- methyl tetrahydrofolate and has responded to treatment with folinic acid. This is sometimes associated with underlying mitochondrial disorders but muscle biopsy in this case did not show any evidence of mitochondrial disease. MRI brain has shown partial resolution of the abnormal signal in the periaqueductal grey matter.

Poster No. 069
Dissecting vertebrobasilar aneurysm in a child

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Introduction: Paediatric intracranial aneurysms are rare. The pattern of disease is different to that in adults and there is far less literature available. I provide a case as an example of the presentation and progress of a child with a dissecting vertebrobasilar artery aneurysm.
Presentation: 11-year-old boy presented to his local hospital with sudden-onset headache, photophobia and vomiting. Bloods and observations were normal – discharged. Symptoms recurred more severely the following day. Managed as meningitis. 4 lumbar punctures were 'bloody' and considered failed. MRI brain 2 days post-admission demonstrated a vertebrobasilar aneurysm. Transferred to the regional Neurosurgical centre.
Transfer to Neurosurgical/Neurovascular centre: Cerebral angiography revealed dissecting vertebrobasilar aneurysm (12×8×10mm). Fusiform component extending beyond AICI/PICA origins. Wide-necked saccular component.
Procedure and progress: Loaded with Aspirin and Clopidogrel. Underwent endovascular procedure the following day – coil embolization, flow-diverting stent to the aneurysm. Ongoing low dose dual anti-platelet therapy. Made an excellent recovery with no neurological deficits. Further imaging – X-ray cervical spine for possible arcuate foramen or atlantoaxial instability, normal. Ultrasound liver/spleen, normal. Discharged home 10 days post-transfer.
Patient background: Past medical history – under the GP for 18 months of headaches. Trauma – significant fall from bicycle 2 years before with forced lateral flexion of the neck. Posited that this may have been a contributing factor in aneurysm development. No significant family history. Lifestyle – an active boy, enjoys weightlifting and motocross. Weightlifting also posited as a contributing factor.
Conclusions: I provide a case which I hope will raise awareness of paediatric intracranial aneurysms and stimulate discussion concerning their management and aetiology.

Poster No. 070
Cavernoma in children: CDDFT experience of two cases

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Aim: To report two cases of Congenital Cavernoma diagnosed in Children presenting with neurological symptoms.
Cases: Case 1: 10-year-old female presented with multiple left facial focal seizures in the form of twitches with full awareness. There was no family history of epilepsy. A typical event was captured lasting 70 seconds during the awake EEG and was reported as focal seizure arising from right hemisphere. An MRI Brain scan showed 2 popcorn balls lesions within the frontal/fronto parietal lobes, one on each side (Right>Left) with evidence of bleeding. She remains seizure free on

Carbamazepine. CCM gene results are awaited and neurosurgeon opinion was not for intervention and for local follow up. Case 2: 12-year-old male had presented with confusion at 7 years of age. He also had transient loss of vision, vomiting, headaches with a few minutes unresponsive episode during admission. With a diagnosis of migraine, he had an MRI Brain scan as OP that showed multiple cavernous haemangiomas in the cerebrum and cerebellum with the largest demonstrating a fluid level in the left parieto-occipital region. Family history revealed that father had seizures secondary to brain cavernomas. He was positive for KRIT1 (CCM1) mutation. Neurosurgeons advised active monitoring and he presented again at 12 years with focal onset seizures with impaired awareness. EEG was normal but MRI showed a new cavernoma in the left temporal horn with bleeding. He remains well on Carbamazepine with a plan for yearly MRI scans.
Conclusions: Congenital Cavernomas of brain can be sporadic or familial, can be multiple and in any location including brain stem and can result in physical disability secondary to bleeding. In the majority of cases bleeding is spontaneous and diagnosed on MRI scans after a neurological event.

Poster No. 071
A FOXing diagnosis: venous ectasia in a patient with FOXP1-related intellectual disability syndrome

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Objective: FOXP1-related intellectual disability syndrome is characterised by developmental delay, variable physical features and autism. Diagnosis has increased with better access to broad genetic testing. We present a case report of a child with FOXP1 mutation whose presentation was notable for significant cerebral venous ectasia.
Case: Child S presented aged 1 year with gross motor delay (not sitting or weightbearing) along with relative macrocephaly (91st–99th centile), strabismus and prominent superficial forehead veins. Intracranial imaging was arranged in which CT angiogram raised a possibility of an arteriovenous fistula. Subsequent catheter angiography excluded this but demonstrated extensive tortuous cerebral venous ectasia. The venous ectasia was not felt to explain her developmental difficulties. Initial genetic testing including microarray and PIK3CA and PTEN analysis was normal. S made some developmental progress but remained globally delayed compared with her peers. Reanalysis of her DNA against a panel of genes associated with intellectual disability identified a de novo heterozygous pathogenic variant in the FOXP1 gene, c.1507C>T, p.(Arg503Ter) (East Anglian Medical Genetics Service).
Discussion: FOXP1 acts as a transcription factor and is likely to be involved in the development of many different tissue types. A wide range of genetic aberrations affecting FOXP1, including point mutations and large structural anomalies, lead to overlapping clinical phenotypes. This patient demonstrates many relevant clinical features including developmental delay with autistic traits, relative macrocephaly with a prominent forehead, strabismus and early gross motor developmental delay. However, descriptions of associated neurovascular anomalies in FOXP1 syndrome are scarce, with a single case report recording a venous angioma and none of cerebral venous ectasia to our knowledge. FOXP1 follow up studies and whole exome or genome sequencing may help determine whether there is an additional genetic cause for this child's cerebral venous ectasia or whether it is FOXP1 related.

Poster No. 072
Paediatric arterial ischaemic stroke (pAIS) 2 years on from the RCPCH guideline: how are we doing?

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Objective: A 2017 RCPCH guideline was published to increase awareness of Stroke in children and standardize best practice. The need for urgent (within 1h) CT angiography in children presenting with suspected stroke and criteria for thrombolysis were set out. We aimed to review the acute management and investigation of pAIS in children (1mo to 16y) since the introduction of the guideline with an emphasis on identifying candidates for thrombolysis.
Methods: Retrospective notes review in a single regional neurology centre over a 20-month timeframe.
Results: Eighteen cases were identified (8F:10M) with two mortalities. Age range 2 months- 13 years (mean 4.8y). 10/18 presented in peripheral hospitals and 8/18 in the regional centre. No cases had pedNIHSS score documented on presentation. 9/18 had dedicated vascular imaging (CTA/MRA) on initial imaging. 12/18 presented with a hemiparesis, 2/18 with seizures, 2/7 dysphasia, 1/7 headache, 1/7 ataxia. 5/18 cases had a stroke post cardiac surgery, 5/18 idiopathic stroke, 3/18 post varicella angiitis, 2/18 arterial dissection, 2/18 cardiomyopathy and 1/18 embolic stroke as a complication of central line insertion. 5/18 presented with an acute hemiparesis with a clear time of onset. No cases received thrombolysis. 1/5 was imaged within 1 hour of presentation. 1/5 had vascular imaging (MRA or CTA) on presentation. 1/5 cases was discussed acutely with Paediatric Neurology; this case was not suitable for thrombolysis due to cardiomyopathy. In retrospect the other 4/5 cases were suitable candidates for thrombolysis.
Conclusions: The results highlight the continued need for enhanced awareness of Paediatric Stroke as a medical emergency. Most acute strokes will present to peripheral hospitals. Therefore, there is a need for regional multidisciplinary integrated pathways amongst Emergency Department Physicians, Paediatricians and Radiologists to

ensure prompt vascular neuroimaging and discussion with a Paediatric Neurologist about the possibility of thrombolysis in suspected pAIS.

Poster No. 073

'A nudge, a fall and a weakness' – a common but missed cause of paediatric stroke

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Objective: This study retrospectively analysed paediatric strokes with further evaluations and outcomes of strokes related to minor injury, to isolate characteristic features and outcomes in these patients.
Methods: Paediatric patients (6mo to 15y age), presenting with acute stroke between January 2015 to January 2019 were retrospectively recruited from a tertiary care hospital in North India. From this cohort, strokes following minor injury were analysed for clinical profile, investigations and outcomes (measured by International Paediatric Stroke Study Scoring System, IPSS).
Results: Of the total 114 cases, 50 (43.8%) were post-minor injury (M: F 2.5:1; mean age 14.2±3.4mo). Of the remaining (n=64; mean age 5±4.5y) most common aetiologies were Moya-Moya disease (n=10, 15%) and transient unilateral arteriopathy (n=8, 12%). The post-minor injury group revealed a median time of 60 minutes from trauma to stroke onset. More than 1/3rd (36%; n=18) had transient episodic hemi-dystonia on the hemi-paretic side after a median of 4 days of symptoms onset. 90% (18/20) of children where results were available had anaemia. CT head in all (n=50) showed calcification of the lenticulo-striate vessels. Subsequent brain MRI (n=20) confirmed CT findings of basal ganglia ischaemia. MR angiogram and thrombophilia screen (n=6) done in the first few patients were normal and hence not pursued subsequently. Follow ups of 44/50 (6–48mo; median=12mo) showed good recovery in the majority (66%; n=29/44). The median IPSS score for these children was 0.5.
Conclusions: Trivial injury leading to basal ganglia stroke was the most common cause of paediatric stroke, occurring exclusively in less than 2 year-olds. CT head was diagnostic (calcification in lenticulo-striate blood vessels and ischemia) with no further information revealed from vascular imaging or thrombophilia work-up. Children were commonly anaemic, a potential causative association. Often transient episodic hemidystonia of the hemiparetic side after a few days was witnessed. Neurological outcomes in most children with this entity is good.

Poster No. 074

Paediatric strokes in South Wales: a case series

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Introduction: RCPCH launched guidance on Paediatric stroke in March 2017. We present a series of paediatric patients who presented with stroke following this publication. We audited this group of patients against the key standards of the RCPCH guidance.
Methods: We retrospectively analysed cases between April 2017 and April 2019. We identified cases from a neurology database and audited acute management using RCPCH guidance 2017 as standard.
Results: We identified 11 children with stroke in the last 2 years. Ages ranged from 21 months to 16 years with a mean age of 8 years at presentation. 7 children had haemorrhagic stroke and 4 had ischaemic stroke. The majority involved the anterior cerebral circulation (10/11). Underlying aetiology was identified in 6 patients, 5 of whom had haemorrhagic stroke. 2 of the patients died. Only 2 out of 11 patients had brain imaging within an hour of presentation. Only one patient was eligible for thrombolysis, however due to contraindication she underwent thrombectomy.
Discussion: Stroke pathways are well developed in adult services. Due to the rarity of stroke in childhood and challenges with recognising symptoms, treatment is often delayed. Symptoms in children need a high index of suspicion. The findings of this audit support the development of an all Wales paediatric stroke pathway. We aim to facilitate activation of the stroke pathway when children present with the FAST symptoms. We also hope to increase awareness of stroke in childhood.

Poster No. 075

Withdrawn.

Poster No. 076
Recognition and clinical pathways for management of acute arterial ischaemic stroke in children

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Objective: Stroke is a common childhood neurological disorder, affecting at least 400 children in the UK each year. The majority of children have residual sequelae across a wide domain of functions, with significant personal and societal consequences. Recent RCPCH guidelines have proposed criteria for hyperacute treatments; this would require rapid recognition of the potential diagnosis by clinicians. Here we describe the acute care pathway of a group of children with confirmed arterial ischaemic stroke (AIS).
Methods: Parents of children aged >28 days and <18 years referred to GOSH (AIS) (2015–2019) were approached and sent a questionnaire exploring their experience of navigating through the healthcare system on initial presentation. Responses were tabulated where possible and reported as frequencies; qualitive results were thematically coded and categorised for analysis.
Results: 41/90 eligible parents responded. 999 and the GP were the first port of call for the majority (n=12 for each). Ten parents stated they had 'no idea' what initial symptoms might represent. When directly asked if they had suspected a stroke, nearly 2/3 stated 'no'. F.A.S.T features (F: face A: arm S: speech T: time) were noted in a third of patients and only 10 patients were given a diagnosis of stroke at first presentation. On initial discharge, a correct diagnosis of stroke was provided to 21 patients. Notably, the need for improved education of paediatric stroke, for healthcare providers was raised by nearly 50% of parents surveyed.
Conclusions: The study demonstrates the need for further education to be delivered in pre-hospital, primary and secondary healthcare settings for recognising acute stroke in children. This will be an essential step in the delivery of hyperacute treatments.

Poster No. 077
Hereditary spastic paraparesis (HSP) – SPG45 NT5C2 mutation

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Background: Hereditary spastic paraparesis refers to a heterogeneous group of inherited neurodegenerative disorders characterized by progressive lower limb spasticity and weakness. There is marked genetic heterogeneity in HSP with all modes of inheritance described for the different loci and causative genes implicated up to now. We present a case of a child with a complex diagnosis of HSP with a homozygous missense mutation in NT5C2 underlying hereditary spastic paraplegia SPG45.
Case presentation: This child had initially been diagnosed as having bilateral cerebral palsy with diplegic pattern and GMFCS II. He had gross motor and speech and language delay. There was a family history of consanguinity. MRI scans had initially been described as showing evidence of periventricular leukomalacia and he had been referred for consideration of SDR. Following tertiary assessment there were clinical concerns that the overall diagnosis may need to be re-explored. Review of his MRI scans demonstrated similarities to a case series of HSP with a rarer form of HSP (SPG45). He subsequently tested positive for SPG45 NT5C2. A second case with similar clinical findings has now been identified in our region. MRI scan findings will be presented.
Summary: SPG45 is a rare but important cause of a cerebral palsy phenotype and testing for NT5C2 should be considered in the differential diagnosis and investigation of patients presenting with CP.

Poster No. 078
Quality of life improvement in a GMFCS V patient following SDR: a family perspective

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Recommendations on patient suitability for SDR has focused on children functioning at GMFCS level II or III. SDR has been considered for GMFCS levels IV and V however the decision to progress can be challenging. The goals in these children are significantly different with the focus being around comfort and pain relief rather than mobility. We describe the case of a boy with a mixed pattern movement disorder involving 4 limbs which had initially been managed with oral medications baclofen, trihexiphenidyl and intramuscular botulinum toxin. Due to the child having a VP shunt the family didn't wish to consider ITB pump. Despite optimisation of oral medications and intramuscular botulinum toxin spasticity was a significant issue adversely impacting on quality of life. Escalation of baclofen was unsuccessful due to loss of head control and duration of action of botulinum toxin injections appeared to be limited to 4 to 6 weeks before tone increased again. This resulted in significant difficulties with moving and handling. In view of this the option of selective dorsal rhizotomy was explored. The goal was to improve ease of personal care and sleep. Post-operative outcomes greatly exceeded the family expectations. Along with a reduction in tone in the lower limbs they were delighted to report several unexpected improvements. These included: Improved functional ability with the left upper limb which facilitated switch access; Improved truncal control making moving and handling easier; A reduction in extension posturing which had been particularly problematic pre-operatively; Significant improvement in sleep; Improved mood. This resulted in the local team exploring eye gaze technology with him. These functional benefits

have significantly improved the quality of life for not only the patient but his family. Further research into the benefit of SDR in this group of patients should encompass care and comfort outcomes, sleep assessment and measurement of pain.

Poster No. 079
Transdermal clonidine in the management of childhood dystonia

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Introduction: Clonidine has become increasingly repurposed for the management of childhood dystonia. One potential advantage of clonidine is the availability of patches for transdermal delivery. We aimed to review the use of transdermal clonidine patches in our institution.
Methods: A retrospective notes review of children and young people (CAYP) with dystonia issued transdermal clonidine patches as identified from pharmacy records.
Results: A total of 45 CAYP were identified, median age at initiation of clonidine of 7 years 5 months (range 10mo to 14y and 5mo). Prior to initiation of patches 43/45 CAYP were already receiving clonidine, including 5 acutely receiving IV clonidine infusions. One child with difficult IV access experiencing an acute deterioration of dystonia was lost to follow up following transfer to local services. The commonest indications for transdermal clonidine were concerns about 'on/off' effect of enteral doses (n=23) and concerns about enteral absorption (n=17). Transdermal Clonidine was discontinued by 5/44 CAYP (3 as patches wouldn't adhere, 1 receiving patches as a temporary bridge from IV to enteral clonidine and 1 due to severe local cutaneous reaction). One additional clonidine naive child experienced significant hypotension with a 0.75μg/kg/hour transdermal dose but tolerated a reduced dose of 0.25μg/kg/hour. Follow up for the remaining 39/44 children ranged from 2 months to 6.5 years (median 1y). The median transdermal dose was 1.67μg/kg/hour (range 0.25–8.05μg/kg/h). Additional enteral clonidine was used by 25/44 CAYP. Efficacy of transdermal clonidine was difficult to determine, but 18/44 CAYP retrospectively scored 2 on the Clinical Global Improvement-Scale, suggesting significant improvement.
Conclusions: In CAYP receiving enteral clonidine switching to transdermal clonidine patches appears to be well tolerated, with 88.6% of CAYP continuing with longer term use. Further prospective work is required to determine the efficacy and safety profile of transdermal clonidine.

Poster No. 080
Intrathecal baclofen (ITB) in the management of hypertonia in childhood – a tertiary centre experience

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Objective: To review the indications for and outcomes following ITB for children and young people (CAYP) at our centre.
Methods: 42 patients were identified undergoing ITB pump insertion from 2006 to 2015. 35 had reports available. A retrospective note review was performed, with data extracted using a standardised data collection proforma.
Results: Median age at ITB pump insertion was 9 (range 4 to 18). Hypertonia was described as dystonia, spasticity and/or dyskinesia. Median length of follow up was 3 years (range: 1mo to 9y). Choice of outcome measure was dependent upon the goals identified for surgery. Care Provider Child Health Index Living with Disability (CPCHILD) data was available for 23 CAYP at baseline and 18 CAYP at 1 year. CPCHILD improved from a median score of 45.5 to 58.2 at 1 year (P=0.03, Wilcoxon signed rank test). Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) data was available for 12 CAYP at baseline (median: 92.5 for motor, 30 for disability), 10 CAYP at 1 year (median 98.25 for motor, median 28 for disability), all with a clinical picture of dystonia. Gross Motor Function Measure (GMFM) was available for 9 CAYP at baseline (median=40), 8 CAYP at 1 year (median 47) and 7 CAYP beyond 1 year (median=43.1). GMFM and BFMDRS were not statistically significant. Pain was measured with paediatric pain profile, available for 14 CAYP at baseline, 6 CAYP in 1 year and 3 CAYP beyond 1 year. Median of most troublesome pain improved from 29 at baseline to 17 in 1 year.
Conclusions: For a heterogeneous cohort of CAYP with motor disorders, ITB appeared to improve ease of care and comfort, indicated by change in CPCHILD. Multiple measures are required to fully capture benefits seen in this cohort, which should be focused on their individual needs for intervention.

Poster No. 081

Neurosurgical interventions for the management of hemidystonia: a systematic review

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Objective: To evaluate neurosurgical interventions and outcomes in the management of hemidystonia.
Methods: The PubMed database was searched including terms 'hemidystonia', Hemi-dystonia', 'Unilateral dystonia', 'Dystonia AND (Pallidotomy OR thalamotomy)', 'Dystonia AND (DBS OR 'Deep Brain Stimulation')' and 'Dystonia AND (ITB OR 'intrathecal baclofen')', up to May 2019. Papers were included if written in English and presenting outcome data for human participants undergoing a neurosurgical intervention for management of hemidystonia. Reference lists of included papers were also reviewed. Individualised patient data was extracted. To facilitate comparison across patients with and without validated dystonia scale scores individual patient outcomes were categorised on a 6-point scale ranging from 'Worsened Compared to baseline' to 'Very marked improvement'.
Results: We identified 53 reports meeting inclusion criteria, describing 144 unique patients (20 <18y of age). Ablative methods (85/144 cases) most commonly targeted the thalamus, and DBS (59/144 cases) the GPi. In recent years DBS is reported far more commonly then ablative surgery. Reported follow up ranged from 6 months to 10 years. One patient underwent ITB but no further individual data was available. Out of the 144 cases 82 had individual outcome data. Objective measures were available in 38 DBS and 7 ablation cases, most commonly the BFMDRS. Reported outcomes in DBS patients were 2/47 worsening compared to baseline, 4/47 no change, 13/47 slight improvement, 10/47 moderate improvement, 9/47 marked improvement and 9/47 very marked improvement. For the ablative cases 0/35 worsened, 12/35 no change, 6/35 slight improvement, 10/35 moderate improvement, 3/35 marked improvement and very marked improvement. Complications were reported in 2 DBS cases (1 shielded battery syndrome, one infection) and 7 ablative cases (2 depression and 5 transient hemiplegia).
Conclusions: Available evidence for the neurosurgical treatment of hemidystonia is of low quality, but suggests generally positive results, with few complications reported.

Poster No. 082

Early results of nerve transfer to restore function in severe acute flaccid myelitis

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Introduction: Acute flaccid myelitis (AFM) is a recently characterised condition causing multiple muscle paralysis and life-changing disability in children. No medical treatment is effective. However, recovery of denervated muscle function is possible via nerve transfer surgery. Such treatment is complex, specific to the individual and should be carried out by specialist teams.
Objective: To describe the clinical features, management and outcomes of nerve transfer surgery following the 2018 AFM outbreak.
Methods: Retrospective analysis of patients with AFM treated with nerve transfer surgery in 2019. Surgical criteria: persistent motor deficits (paralysis) 6 months post onset with neurophysiologic signs of denervation and donor nerve availability.
Results: Eight patients (M=F, aged 26–75 months; mean 40) were referred between March and July 2019. At initial onset/infection: 6/8 had involvement of all four limbs and trunk and 4/8 had involvement of the phrenic nerve. Mean date of initial assessment within specialist centre was 10.5 months post onset (range 4–38). At this time 7 had upper limb paralysis (4 Right, 3 Left) and 1 had bilateral lower limb paralysis. Following consultation, 1 declined surgical intervention and 2 are awaiting surgery. 5/8 patients have proceeded to surgery: 4/5 cases presented with three-or-more nerve root involvement. 10 nerve-transfers have been performed (median 2 per patient). No surgical complications were encountered. Early clinical functional outcomes from this cohort following surgery are currently being collated and evaluated and will be presented in full at conference.
Conclusion: This study supports international experience that nerve transfer surgery can improve functional outcomes in AFM. The delivery of care in the NHS requires coordination and referral to specialist centres. Experiences with this cohort will inform decision making and improve patient outcomes and family expectations during the next outbreak of AFM.

Poster No. 083

A catastrophic case of acute flaccid myelitis

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Objective: Acute Flaccid Myelitis (AFM) is a rare but serious neurological condition characterised by acute onset of flaccid weakness in one or more limbs with distinct abnormalities of the spinal cord grey matter on magnetic resonance imaging (MRI) and without any features suggesting an upper motor neuron disorder. In recent years, there has been a global increase in the incidence of AFM associated in some cases with a non-polio enterovirus, EV-D68. The long-term prognosis in most cases remain poor. We present a severe case of AFM in a 3-year-old boy with catastrophic consequences.
Method: Retrospective review of clinical course, neuroimaging, treatment and neurorehabilitation.
Results: A 3-year-old boy presented with clinical encephalitis. He deteriorated over 24 hours and developed an encephalopathy, multiple cranial nerve deficits, and complete flaccid paresis requiring PICU support. CSF 2 weeks apart showed a resolving lymphocytic pleocytosis with increased protein (0.5 to 0.92 g/dL). Serial MRI brain and spinal cord showed

extensive signal abnormality involving thalamus, dorsal pons, medulla, cervical cord, conus along with cauda equina. Nerve Conduction Studies were consistent with a severe acute motor axonal neuropathy. EEG showed a posterior dominant encephalopathy. Infective (including EDV-68), metabolic, immunological (AQP4 and MOG Abs) and genetic (RANBP2) tests were negative. Immunomodulation therapies (Methylprednisolone, IVIg, and plasma exchange) resulted in no clinical improvement. Resolution of signal changes in the thalami, brainstem and spinal cord along with mild generalised cerebral atrophy was noted in repeat MRI after 3 months. 10 months following presentation he remains fully ventilated with no significant motor improvement despite intensive rehabilitation including use of passive range of movement devices and functional electrical stimulation.
Conclusion: This is one of the most severe cases of AFM, representing the wider spectrum of AFM involving encephalopathy, dominant bulbar signs and quadriparesis.

Poster No. 084
Mirror movement disorder

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Mirror movement disorder (MMD) is a rare movement disorder with a prevalence of less than 1 in a million in which involuntary symmetrical movement is observed in the limb contralateral to the voluntary limb movement. We report 2 children with an MMD. Case 1: A 15-year-old girl following an uneventful pregnancy and normal delivery, born to non-consanguineous parents presented with difficulties with fine motor activities like writing. Parents noticed from age of eight that her left hand would make similar movements to her right hand in activities like writing, combing etc. Maternal grandfather has MMD. Case 2: A 9-year-old girl following an eventful pregnancy and normal delivery to non-consanguineous parents presented with an MMD at age of 5 years first noticed whilst writing and this continues affect her activities of daily living. There is no family history of MMD. Both children are neurodevelopmentally normal and have normal MRI brain and spine. MMD have been described congenitally due to prenatal insult before 28 weeks gestation, Kallman Syndrome and Klippel-Feil syndrome or as an acquired due to hemiplegic stroke and Parkinson's disease in adults. Pathogenesis is thought to be due to lesions in supplementary motor area, corpus callosum or cervical lesions. Mutations in DCC and RAD51 gene are present in 35% of the cases. The multimodal MRI and neurophysiological studies have revealed that the motor system is completely disorganised with abnormal crossing at brain stem level and abnormal communication between both brain hemispheres in these children. There is a positive family history in some cases. The upper limbs are commonly involved. Diagnosis is usually clinical and treatment is symptomatic with support at school and limiting repeated complex and sustained movements involving both hands.

Poster No. 085
Acute spinal cord infarction in children: a review of the presentation, aetiological investigations and outcomes in 6 children

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Aims: Acute spinal cord infarction is poorly understood in the paediatric population. We reviewed cases presenting to a single paediatric neurology centre in UK between 2010 and 2019 to explore common themes of presentation, aetiology and outcome.
Material and methods: Cases of spinal cord infarction presenting to a single centre were identified from our spinal database and medical records were reviewed to determine clinical presentation, aetiological investigations, management and outcomes.
Results: Six children/young people were identified, 2 male, 4 female, age range 3 to 14 years. 4 participants presented with symptoms after seemingly trivial movements or trauma, including: being kicked in the back whilst playing football, bending forwards to tie hair up, getting up to walk in the garden, and performing a crab gymnastic movement. 2 had no obvious precipitants. Initial presentation was neck or back pain in all patients, progressing to bilateral lower limbs weakness, sensory deficit, lost reflexes, and urinary/bowel involvement. MRI imaging failed to reveal the diagnosis when performed early in 1 participant. The level of lesions for each participant were: T2-3; T2-6; T2-T12; C2-T6; C1-T8; and isolated to the conus. Aetiological investigations, including thrombophilia screens, failed to reveal a cause in any participant. 2 initially received steroids because the differential diagnosis included an inflammatory disorder. 2 patients received aspirin, 5/6 gained motor improvement but none returned to normal. All had residual bladder problems, 5 had bowel sequelae.
Conclusions: Spinal cord infarction may be related to minor trauma or movements. The association with a Chiari 1 malformation is previously described in adults. Outcome is poor. Although motor improvement can be seen, children do not return to normal functionally. Aetiological investigations and treatments vary within a single centre. National recommendations are required to standardise practice.

Poster No. 086
Cost of care for long-term ventilation patients

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Background: Advances in Neonatal and Paediatric Intensive Care have increased the survival of children with life threatening or life limiting conditions. There has been a significant rise in children on long-term home invasive ventilation. High profile cases have been in the media recently with debate on whether such interventions should be implemented focussing on ethics but without evidence of cost benefit analysis.

Children on long-term invasive ventilation are a high cost group with complex and varying underlying medical conditions requiring input from multiple teams, including 24 hour carers, medical and multidisciplinary team input as well as recurrent hospital and PICU admissions. In addition, the cost of equipment and drugs makes this a costly intervention. In any limited healthcare system rationing decisions have to be made: drug and other therapies are subject to health economic analyses. This study aims to assess cost per annum for LTV and a cost benefit analysis.
Objective: Identify patients on LTV including comorbidities. Assess cost of LTV to quantify cost-benefit analysis. Measure outcomes: death/admissions/recovery.
Methods: Review of patients requiring home long-term invasive ventilation July 2009-July 2019. Analysis of costs: clinic visits, hospital admissions, costs of equipment; cost of medication. Outcomes and quality of life: mortality, admissions and length of stay; decannulation, ability to communicate and mobility analysis; ability of parents to work.
Results: 9 patients: 3 died (aged 1, 7 and 15y), 4 decannulated, 3 ongoing LTV (aged 15mo, 19 and 22y), 5 night package £140 000 pa, accessories £12 000 pa, replaceables/service £92 000, average cost home LTV around £350 000 pa.
Conclusions: LTV ventilation is an expensive treatment: its use should be analysed on a cost benefit analysis in a similar way to other available treatments.

Poster No. 087
The use of amplitude integrated electroencephalography (aEEG) in preterm neonates within a neonatal intensive care unit: a feasibility study

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Objective: To assess the feasibility of recruiting to a study, performing and interpreting aEEG in preterm infants, and to assess family and staff members' views.
Methods: A prospective feasibility study. 7 preterm neonates between 26 and 30 weeks postmenstrual age were recruited for continuous aEEG monitoring using adhesive electrodes whilst receiving NICU care. We studied optimal methods of attaching leads, impedance data, number of electrode changes, and preliminary aEEG findings. Staff and parents were asked for feedback on the process and their involvement.
Results: We recruited 36.8% of eligible babies. NuPrep and Sorbaderm were the most effective combination for skin preparation. The aEEG recording was good quality if staff were engaged and knew when electrodes needed to be changed. Four of the seven (57.1%) babies showed seizure activity on aEEG, none of which were diagnosed clinically. Babies with seizures were born earlier, had lower birthweights, and had more complications than babies without seizures. Feedback showed parents and staff were positive, although staff reported caring for the baby was harder. 75.0% of parents and 87.5% of staff would 'definitely' recommend the study to parents with a premature baby.
Conclusions: The use of continuous aEEG in preterm neonates in feasible, with similar recruitment rates to other studies in the department, and a positive experience for parents and staff. A high rate of electrical seizures was detected.

Poster No. 088
Variation in prognosis given by feto-maternal units in fetuses with neurological abnormalities

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Background: The 'Magnetic Resonance Imaging (MRI) to enhance the diagnosis of fetal developmental brain abnormalities in utero' (MERIDIAN) study showed improved diagnostic accuracy and confidence for detecting fetal neurological abnormalities compared to ultrasound. The additional information provided by in utero MRI altered prognosis in 44% of women. The MERIDIAN study did not report whether the neuro-developmental prognoses given to women varied between clinicians or were accurate.
Objectives: To assess the variation in prognosis given to pregnant women by clinicians in Feto-Maternal units for 5 different fetal brain abnormalities.
Methods: We contacted one clinician at each of the MERIDIAN Feto-Maternal Units and asked what percentage chance of normal neuro-developmental outcome they would give pregnant women for 5 fetal neurological abnormalities: isolated ventriculomegaly 10 to 12 mm; Unilateral hypoplasia of the cerebellar hemisphere, Isolated hypoplasia of the cerebellar vermis, Isolated Cisterna Magna, and Isolated Blake's Pouch Cyst. Respondents were asked to give a percentage chance of normal outcome, although some used free text to answer.
Results: Responses were received from 14 senior obstetricians in 14 Feto-Maternal Units. There was general agreement for isolated mild ventriculomegaly with respondents replying that 90 to 95% would have normal developmental outcome. Wider variation was seen for posterior fossa abnormalities, with the suggested chance of normal outcome for one condition ranging from 10 to 90%.
Conclusion: Estimating long-term neuro-developmental outcome based on antenatally detected neurological abnormalities is challenging due to limited high-quality data. Our data highlights there is high variation in outcomes offered by different clinicians for the same abnormality. Further work is needed to determine what advice is given by obstetricians on the potential developmental outcomes of a wide range of fetal brain abnormalities in current practice, how well these agree with published evidence, and whether the involvement of paediatricians with experience in neuro-developmental disorders improves prognostication.

Poster No. 089

Accuracy of in-utero MRI to detect fetal brain abnormalities and prognosticate developmental outcome: postnatal follow-up of the MERIDIAN cohort

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Background: In-utero MRI (iuMRI) detects fetal brain abnormalities more accurately than ultrasonography (USS) and provides additional clinical information in around half of pregnancies. There is little published data on whether postnatal neuroimaging beyond 6 months of age changes the diagnostic accuracy of iuMRI nor its ability to predict developmental outcome.
Methods: Families enrolled in the MERIDIAN Study whose child survived to 3 years of age were invited to have a case note review and assessment of developmental outcome with either the Bayley Scales of Infant and Toddler Development, the Ages and Stages Questionnaire or both. A paediatric neuroradiologist, blinded to the iuMRI results, reviewed the postnatal neuroimaging if the clinical report differed from iuMRI findings. Diagnostic accuracy was recalculated. A paediatric neurologist and neonatologist categorised participants' development as normal, at risk, or abnormal, and the ability of iuMRI and USS to predict developmental outcome were assessed.
Results: 210 participants had case note review, of whom 81 (38.6%) had MRI after 6 months of age. The diagnostic accuracy of iuMRI remained higher than USS (absolute difference=25%, 95% CI 21% to 29%, $p<0.0001$). Developmental outcome data was analysed in 156 participants: 111 (71%) were normal, of whom 56 (51%) had a normal or favourable prognosis on USS and 76 (69%) on iuMR (difference in specificity=18%, 95% CI 7% to 29%, $p=0.0008$). No statistically significant difference was seen in infants with abnormal outcome (difference in sensitivity=4%, 95% CI –10% to 19%, $p=0.727$).
Conclusions: iuMRI remains the optimal tool to identify fetal brain abnormalities. It is less accurate at predicting developmental outcome, although iuMRI is better at identifying children with normal outcome than USS. Further work is needed to determine how the prognostic abilities of iuMRI can be improved.

Poster No. 090

Introducing hypothermia or not decision algorithm (HONDA) guideline in the assessment of neonates following hypoxic insult at birth in a district general hospital

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Introduction: Hypoxic-Ischaemic Encephalopathy (HIE) accounts for up to 30% of cases of cerebral palsy. HIE can be caused by multiple events and occurs in 2/1000 births. Hypoxic insult at the time of birth can result in an encephalopathic state characterised by: need for resuscitation at birth, neurological depression, seizures and electroencephalographic abnormalities. The Toby Study demonstrated that induction of moderate hypothermia within 6 hours of birth for 72 hours duration in infants who had perinatal asphyxia resulted in improved neurologic outcomes in survivors. Therapeutic hypothermia is the only proven neuroprotective treatment for HIE. An assessment tool was required as there was no standard proforma for neurological assessment for babies with a low cord pH (<7.1) in our District General Hospital (DGH). This was to ensure that all infants who met the TOBY criteria received the appropriate treatment within the recommended timeframe.
Methods: The HONDA assessment tool was developed for use in the tertiary Neonatal Intensive Care Unit. This assessment tool was adapted to use in a DGH as a guideline. The HONDA included the criteria from the TOBY study with a user-friendly flow chart. A comprehensive neurological examination is outlined with text and images to ensure reliable and repeatable findings by different clinicians over time.
Results: The HONDA tool ensured a standard Algorithm was used to assess those infants who had a hypoxic insult at birth. It has standardised record keeping and repeated neurological examination of at-risk infants.
Conclusions: The HONDA is a comprehensive and user-friendly algorithm to ensure those infants who meet requirement for therapeutic hypothermia are being appropriately identified and treated.

Poster No. 091

Foetal exposure to misoprostol and mobius syndrome

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Background: Mobius syndrome is a rare condition comprising a collection of specific congenital anomalies, usually congenital lower motor neuron 6th and 7th cranial nerve palsies. Hydrocephalus, cerebellar hypoplasia, orofacial and limbs deformities have been reported in some. The literature links Mobius Syndrome to early foetal exposure to Misoprostol, a synthetic prostaglandin E analogue widely used for medical termination of pregnancy. For abortions it is used by itself or with the anti-progestogen Mifepristone; the combination is 97% effective during the first trimester of pregnancy. The mechanism

by which misoprostol disrupts brainstem development resulting in hypoplasia or absence of central brain nuclei is not elucidated as yet. Suggested mechanisms include selective vulnerability to hypo-perfusion and ischaemic injury of the foetal brain stem due to direct disruption of the foetal vasculature or to global foetal hypoxia because of uterine contractions and placental ischaemia.
Clinical case: We report a case of an infant with known exposure to Misoprostol from failed medical termination of pregnancy (TOP) at 12 weeks gestation, who presented with an abnormally increased head circumference, multiple lower motor neuron cranial nerve palsies (7, 11 and 12th cranial nerves). His MRI scan showed hydrocephalus due to cerebral aqueduct stenosis, inferior vermian hypoplasia and loss of bulk of the right facial collculus of the pons.
Conclusions: It is vitally important to counsel expectant mothers following exposure to misoprostol and failed TOP of possible congenital anomalies if the woman elects to continue with the pregnancy.

Poster No. 092
Neurological examination in unwell neonates: health care professionals' perspectives

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Objective: To explore health care professionals' opinions of neurological examination in unwell neonates.
Methods: A questionnaire designed to assess views on examining unwell neonates neurologically was distributed to all UK neonatal and paediatric neurology units. Questions included Likert scales, with scores ranging from 0 to 6. Scores of 4 to 6 were taken to be positive, 1 to 3 negative or equivocal. Answers were compared between consultants and other staff members using Chi-Squared testing, with $p<0.05$ assumed statistically significant.
Results: 192 responses were received, although not every question was answered. 106/192 (55.2%) responders were based in general paediatrics, 60/192 (31.3%) in tertiary neonatal units, and 18/192 (9.4%) in paediatric neurology. 92/192 (47.9%) were consultants. 59/192 (30.7%) performed a neurological examination in all unwell neonates, 114/191 (59.7%) in most. 84.8% of consultants felt confident performing a neurological examination, compared to 57.0% of other health care professionals ($p<0.05$). Consultants were also more confident at interpreting the *Results* and using them to formulate management and prognosis (all $p<0.05$). 140/192 (72.9%) did not find a high-quality neurological examination documented routinely in medical notes of half or more unwell neonates. 86/167 (51.5%) reported using the Classical neurology examination adapted for neonates, 22 (13.3%) used the Hammersmith Neonatal Neurological Examination or an adapted version. The most difficult aspects were fundus and cranial nerve examination. The most frequently cited challenges were: effect of medication; difficulties in interpretation; equipment and lines; experience; time limitations; and risks of handling unwell neonates. 124/171 (72.1%) wanted a new standardised neurological examination for unwell neonates; 9 (5.2%) did not.
Conclusions: Non-consultant grade health care professionals feel less confident performing a neurological examination in unwell neonates. All responders highlighted a number of challenges to performing and interpreting the results. Around three-quarters of responders want a new, standardised neurological examination for unwell neonates, which could address these challenges.

Poster No. 093
Use of re-standardised Griffiths Scales of Child Development (3rd edition) in a healthy cohort at 4 to 5 months of age

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Objective: The Griffiths Scales of Child Development (GSCD) is an established tool for the developmental assessment of children from birth to 6 years. In 2016, the GSCD underwent significant revisions, and was re-standardised using contemporary cohorts. To date, no studies have reported on its use in healthy children post-marketing. Our aim is to examine the use of the GSCD-III in a healthy population of infants aged 4 to 5 months and to provide the first published data on the use of the revised Griffiths-III.
Methods: In a prospective observational study of healthy, full-term infants, participants were recruited into a randomized controlled trial of infant massage. Griffiths III assessments were performed by ARICD-trained practitioners across 5 subscales and a general development quotient (GD) at 4 to 5 months.
Results: 178 children were considered in the analysis, male: female ratio 101/77. Mean (SD) birth weight was 3.53 (0.46) kg and mean birth gestational age was 39.8 weeks (SD 1.22). Mean (SD) age at assessment was 4.5 (0.3) months, with 98 (55.1%) children being assessed according to 4/12 rounded norms, and 80 (44.9%) to 5/12 norms. No difference was found in either arm of the study in any subscale. Scores were considerably greater than average (DQ 90–109) in all subscales but particularly subscales B, D and GD. Mean (SD) developmental quotients (DQ) in A=121.0 (15.9); B=130.7 (11.6); C=119.0 (9.7); D=127.0 (8.4); E=123.3 (11.1) and in GD=128.3 (10.1). Using the published cutoffs, we found that 97.2% (n=173) of our cohort scored 'above average' or greater in GD.
Conclusions: We have provided the first data on the use of Griffiths-III in a healthy cohort. Scores were higher than expected across all sub-scales. This may be due to the characteristics of our cohort but raises concern that Griffiths-III may overestimate ability in young infants.

Poster No. 094

Review of metabolic investigations at Tallaght University Hospital, Dublin, Ireland

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Objective: Metabolic investigations are important in the investigation of children with disordered development. The aim of this audit was to determine if paediatric metabolic investigations were ordered as per current best practice evidence at Tallaght University Hospital, Dublin, Republic of Ireland.
Methods: We used recommendations from seven publications to guide this audit and identified indications for performing metabolic investigations. We reviewed metabolic investigations sent on paediatric patients at Tallaght University Hospital from 1 January 2018 to 31 December 2018. We identified the clinical indication for investigating patients by reviewing dictated clinic letters available on the hospital intranet and confirmed investigation results by reviewing scanned copies available on the hospital intranet. We compared the indications for metabolic investigations with published expert guidelines.
Results: Metabolic investigations were performed on 254 patients from 1 January 2019 to 31 December 2018. Six patients had inconclusive results and were referred to the Metabolic Team at Temple Street Children's University Hospital Dublin for further assessment. There have been no metabolic diagnoses made to date as per Tallaght University Hospital dictated letters.

Of the 254 patients, 104 had a diagnosis of Autism Spectrum Disorder (ASD). Of those with ASD, 33 had a confirmed or suspected intellectual disability. 158 patients (62%) met best practice recommendations for metabolic investigations. Of the 96 patients who did not fulfil recommendations, 71 (74%) were for children with ASD.
Conclusions: We identified two areas that could improve patient care by optimising diagnostic yield and improving resource utilisation at the hospital. First, we recommend clinicians send targeted investigations and avoid blanket investigations for children with disordered development, including ASD. Second, we recommend clinicians include relevant clinical details on request forms to improve diagnostic yield. Finally, we question the value of metabolic investigations for intellectual disability in the absence of other clinical risk factors or comorbidities and suggest this requires further study.

Poster No. 095

The early developmental course of babies with Sturge-Weber syndrome

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Background: Sturge-Weber syndrome (SWS) is a rare neurocutaneous condition which arises from a mutation in G Protein Subunit Alpha Q. The hallmark is leptomeningeal angiomas often associated with a facial port-wine birthmark. Seizures, stroke-like episodes and hemiplegia are common clinical presentations.
Objective: To describe clinical features of infants with SWS under 3 years and their developmental trajectory in relation to seizure onset.
Methods: A retrospective case note review was conducted on 90 children aged below 3 years with SWS under clinical review at our centre. The medical history and standardised developmental test results (language, cognition, motor and visuospatial skills) contained in patients' assessment reports were analysed.
Results: Common clinical features of children with SWS aged under 3 years were: seizures in 81 patients (90%), hemiplegia in 52 patients (57.8%) and glaucoma in 42 patients (46.7%). Their developmental trajectory was a decrease in the mean percentiles (for language, cognition and motor skills) and mean developmental quotients (for visuospatial skills) over the first 36 months. Infants with unilateral brain involvement had significantly higher cognitive percentiles than those with bilateral brain involvement ($p<0.01$), but both groups showed the aforementioned pattern. Children with epilepsy had worse language ($p=0.039$) and cognitive outcomes ($p=0.004$) than children without seizure onset.

There was seizure onset in the first year in 62 infants (78.5%). In these patients, earlier seizure onset was associated with a higher language percentile ($p=0.041$) at age 36 months or at the time of seizure onset.
Conclusions: Following treatment of early seizures in SWS language recovery appears to occur over time relative to cognition. The functional plasticity of language might account for these observations. It is proposed that seizure prevention and optimal seizure control in the crucial first year of life will benefit cognitive and language development in patients with SWS.

Poster No. 096

An atypical case of Rett syndrome with new insights on disease mechanisms: description of early onset features before regression and evidence of associated mitochondrial dysfunction

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Objective: Rett syndrome (RTT) is a rare neurodevelopmental disorder primarily affecting females, characterized by loss of speech, stereotypies, abnormal hand movements, motor and cognitive impairment. Diagnosing RTT before regression occurs remains a challenge and there is an increasing interest in early diagnosis, due to the ongoing gene therapy clinical trial in RTT.
Methods: Retrospective case notes review. The patient was born at term after induction of labour for reduced movements, with meconium-stained liquor, but was well. Poor crying and suck noted at birth with gradual deterioration of feeding, with frequent chest infections, necessitating PEG-

feeding at 6 months. Peripheral/axial muscle weakness and hypotonia were noted at this time. MRI brain showed mild underopercularisation of sylvian-fissures; thin corpus-callosum. MRS, MRI spine, echocardiogram, and EEG were normal. Vitamin B12 deficiency was found, treated with hydroxycobalamin. Sleep study showed hypoventilation with frequent apnoeas and low respiratory rate, leading nocturne BiPAP. EMG was myopathic. Muscle biopsy showed marginal loss of complex-I activity in the respiratory-chain-enzymes analysis.
Results: Videofluoroscopy showed delayed swallow and disorganised pharyngeal stage leading to PEG feeding. Over the following months, no regression noted but only minimal motor progression seen; she was interactive and smiled. At 12 months, regression in her motor abilities was noted – she stopped fixing, following and smiling with progressive microcephaly and hand writhing movements. EEG showed epileptic encephalopathy with tonic/myoclonic jerks. Whole-exome-sequencing showed a de-novo pathogenic mutation in the MECP2 gene (NM_004992.3:c.1157_1200del,p.[Leu386fs]) and the diagnosis of RTT was confirmed. After 3 months, she restarted smiling and fixing/following and making motor progress but continues to have seizures.
Conclusions: This case illustrates early-onset features in atypical RTT with central breathing abnormalities, bulbar insufficiency, generalized hypotonia before regression. Evidence of mitochondrial dysfunction is in keeping with recent reports suggesting neuronal redox imbalance in RTT as one of the disease pathogenic contributors.

Poster No. 097
Early-onset presentation of a new subtype of β-propeller protein-associated neurodegeneration (BPAN) caused by a de novo WDR45 deletion in a 6-year-old girl

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Objective: Neurodegeneration with brain iron accumulation (NBIA) comprises a group of rare genetic disorders characterized by progressive extrapyramidal and other neurological symptoms due to focal iron accumulation in the basal ganglia.1 β-Propeller protein-associated neurodegeneration (BPAN) is the most recently identified subtype of NBIA caused by heterozygous variants in WDR45 at Xp11.23. We report a new subtype of BPAN caused by a de novo WDR45 variant in a 6-year-old girl.
Methods: Case report on a new subtype of β-Propeller protein-associated neurodegeneration (BPAN) caused by a de novo WDR45 deletion in a 6-year-old girl and review of the literature.
Results: We report a 6 year old girl with BPAN due to a large (5824 bp) de novo chrX:g.48,930,034_48,935,858del (hg19) deletion in WDR45, presenting with early-onset global developmental delay, hypotonia, seizures, and speech apraxia. The patient presented at the age of 10 months with hypotonia and motor developmental delay, following a normal birth history, and at 14 months developed complex partial seizures and later on steroid-responsive electrical status epilepticus of slow-wave sleep (ESES). She has made minimal developmental progress and has remained profoundly globally developmentally delayed and cognitively impaired, and has still not achieved independent ambulation.
Conclusion: We have described the clinical, neurophysiological and neuro-imaging findings in a 6-year-old girl, the unique combination of which may assist in the diagnosis of further similar cases. BPAN is an exceedingly rare, severe and debilitating disorder with a broad spectrum of clinical heterogeneity and variable age at presentation with early-onset symptoms. Early detection and diagnosis are very important in order to offer proper genetic counselling to affected families and provide symptomatic treatment to patients. Next-generation broad-spectrum genetic analyses will enable early detection of BPAN in the paediatric age group in order for patients to be diagnosed prior to reaching adulthood.

Poster No. 098
I-BAC-DRV: yes technology can

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Introduction: How to measure the effectiveness of an early intervention program in low resource setting. Can assessments lead to interventions? And with improvements leads to new interventions, can new assessment lead to new interventions? Can this system be measured for its effectiveness and improved based on feedbacks and results? An attempt to set up child development centres in low resource countries using software, Apps and e-learning.
Method: 5 years of data in early interventions was analysed in Lucknow, India. In phase 1, 527 children with non-progressive neurological problems were given best available local interventions. Only 8% compliances and improvement were seen. Based on the feedback algorithms were written to create individual profile of children based on their skills (UK Curriculum of excellence), disability score, information processing preference, educational and behaviour problems. Based on the score each child generates an individualised profile and an intervention plan delivered by App for parents (P-BAC-DRV) and App (T-BAC-DRV) at child development centres. The assessment is repeated every 2 months and new individualised profile is generated with new set of intervention. In total more than 2000 interventions are developed, and the algorithm helps in deciding which main areas to target at one time.
Result: The current system in low resource settings have either no service or results are close to 10% prevent disability in non-progressive neurological problems. Our system has shown to prevent disability in about 60% of children. Supported by Government start up initiative the program has won in top 40 data innovations in India.
Conclusion: Use of technology to provide training, exams and support professionals in the low resources areas is the solution to provide effective services. Pattern recognition is the key delivered by software and Auto audits has been placed to measure and improve the system.

Poster No. 099

Introduction of a specialist neuro-oncology physiotherapy role: a 2 year charity funded pilot within Southampton Children's Hospital

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Introduction: Medical advances in the treatment of CNS tumours has enhanced survival but also impacted on levels of residual morbidity and participation.

Service provision has not increased alongside the improvement in survival, with many patients not being able to return to their previous level of activity and participation following their oncology treatment. NICE Cancer services for children and young people 2014 state: 'Children and young people who have had a central nervous system malignancy should receive a specialist neuro-rehabilitation care package'.

Robbie's Rehab, a charity funded physiotherapy service embedded within the Southampton children's hospital therapy service, launched June 2017, provides supplementary physiotherapy for children diagnosed with brain and spinal tumours under the care of Southampton Children's Hospital.

Objective: To accurately identify and quantify the need for this service.

Method: Prospective data was collated and reviewed June 2017–May 2019.

Results: Year 1: 30 patients; Year 2: 32 patients. 94 new episodes of physiotherapy (average 3.9 per month), 303 direct clinical contacts. Reasons for accessing the service: need for enhanced intensity of rehabilitation on discharge (n=23), enhanced inpatient rehabilitation (n=18), bridge the gap whilst awaiting community services (n=11), change in symptoms (n=12), pre-op assessment (n=5), support for palliative care planning (n=7), support for complex social and emotional needs (n=8), disease progression (n=7), higher level rehabilitation not fulfilling community criteria (n=12), facilitate access to local exercise facilities (n=13), within oncology clinic for assessment/one-off treatment (n=8), post-op assessment (n=11), individualised goal orientated participation (n=4). 8 patients had an estimated 2 weeks reduction in acute bed days.

Conclusions: Robbie's Rehab referrals are for a variety of multifactorial reasons with rereferral often needed within their pathway. It has enabled earlier discharge, improved transition to community services and opportunities for therapy access previously not available.

Poster No. 100

Pathogenic GARS variant associated with infantile onset spinobulbar muscular atrophy

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Introduction: We describe a novel case of infantile onset spinobulbar muscular atrophy (SBMA) associated with a likely pathogenic heterozygous missense variant c. 631T>C, p.(Cys211Arg) in the GARS gene.

Methods: Inherited Peripheral Neuropathy Gene Panel next generation sequencing.

Results: Our proband presented at 5 weeks with marked stridor and bulbar weakness after a normal pregnancy. He subsequently developed respiratory failure requiring Nocturnal BiPap and was found to have a Type I Laryngeal Cleft. Initially he met developmental milestones but at 5months developed features of axial weakness with further regression at 9months with limb weakness and loss of deep tendon reflexes. EMG confirmed denervation in genioglossus, as well as proximal and distal limb muscles without evidence of neuropathy. Genetics for SMN1 gene and SMARD were negative. Inherited Peripheral Neuropathy 56 gene panel testing identified a heterozygous missense variant c. 631T>C, p.(Cys211Arg) in exon 5. The variant is predicted to alter a highly conserved amino acid, has not been reported before and has not been identified in control databases. In silico prediction tools supports the pathogenicity of the variant. Mutagenesis of the equivalent amino acid in mice produces impaired motor control and denervation.

Conclusions: The GARS gene encodes an ubiquitously expressed glycyl tRNA synthetase which has an integral role in protein synthesis in all eukaryotic cells. Missense GARS mutations can lead to distal hereditary motor neuropathy as well as a sensorimotor neuropathy phenotype (CMT2D) typically with adolescent or early adulthood onset. There have been 2 cases in the literature to date describing infantile onset. We postulate that the previously undescribed heterozygous GARS variant c. [631T>C]; p. [Cys211Arg] is responsible for infantile SBMA in our proband.

Poster No. 101

Spinal muscular atrophy – a case series of floppy children

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Objective: To discuss SMA, which is one of the differentials in a hypotonic child and bring to light the diagnosis is not always Cerebral palsy (CP).

Method: Descriptive case report.
Results: Case 1: 4-month-old girl admitted to ICU with severe pneumonia.

Case 2: 9-month-old boy, both admitted to the Intensive Care Unit with severe pneumonia. Case 3: 15-month-old girl, presented to outpatient with progressive 'floppy' limb weakness and swallowing and breathing difficulties.

Case 4: Attended OPD with worsening respiratory distress, difficulty feeding, difficulty managing secretions. All 4 had perinatal histories of uncomplicated deliveries but subsequent early respiratory distress and oxygen requirement for the first few days of life. All had been 'floppy' since birth, with severe gross motor delay, feeding difficulties, poor weight gain and recurrent chest infections. Cases 2, 3 and 4 had been diagnosed with CP despite having normal neuroimaging. Examination of all 3 children was similar and consistent with clinical diagnosis of SMA. Findings included an alert, interactive child; frog-legged posture; 4-limb hypotonia and weakness with legs more affected than arms; absent deep tendon reflexes; bell-shaped chest; and tongue fasciculation. Genetic testing for all confirmed homozygous deletion of exon 7 of the SMN1 gene. In all the cases Creatinine Kinase levels were normal, ruling out myopathy.
Conclusions: The incidence of SMA is 1/10 000 livebirths. It can be diagnosed clinically from pathognomic features when genetic testing is unavailable and should be considered in any hypotonic child, irrespective of perinatal history. A wide clinical spectrum that ranges from early death to near-normal adult life exists. Families must be counselled regarding implications of this genetic diagnosis. Correct early diagnosis and multidisciplinary intervention can vastly improve outcomes.

Poster No. 102
SYROS study – long-term reduction in rate of respiratory function decline in patients with Duchenne muscular dystrophy (DMD) treated with idebenone

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Respiratory function decline in DMD is caused by the underlying weakness and degeneration of the respiratory muscles leading to impaired inspiratory and expiratory effort and associated complications. Idebenone reduced the rate of respiratory function decline over 52 weeks in the Phase III DELOS trial. SYROS is a long-term study in former DELOS patients who transitioned to idebenone under Expanded Access Programs following a variable untreated period. Here, we aimed to characterize the long-term effects of idebenone on respiratory function.

Patients were managed according to routine clinical practice. Respiratory function was assessed by calculating the annualized decline in forced vital capacity (FVC) and peak expiratory flow (PEF), expressed as percent predicted (%p). Comparisons were made between treated and untreated periods and to matched external controls. Data on bronchopulmonary adverse events (BAEs) and hospitalizations were collected. Data from 18/64 former DELOS patients were available. At DELOS baseline, mean (SD) age and FVC%p were 13.3 (2.7) years and 58.7% (17.6%); all patients were glucocorticoid non-users and 83.3% were non-ambulatory. Patients were treated for an average (min-max) of 4.2 (2.4–6.1) years compared to an average untreated period of 2.1 (1.1–5.5) years. The annual rate of FVC%p decline was almost halved (3.8% vs 7.4%) when comparing these periods. For the external comparisons, declines remained lower across all treatment years (up to 6y) compared to the matched group of untreated patients. Comparable results were seen for PEF%p. The risk of BAEs was reduced by 68% during long-term idebenone treatment versus untreated periods, leading to fewer hospitalizations due to respiratory causes (0.06 vs 0.15 events per year). Long-term treatment with idebenone results in a consistent and sustained reduction in the rate of respiratory function decline for up to 6 years.

Poster No. 103
Consistent long-term effect of idebenone in reducing respiratory function decline in advanced patients with Duchenne muscular dystrophy (DMD)

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Two placebo-controlled trials of 52-week duration (Phase II DELPHI, Phase III DELOS) showed that idebenone consistently reduced respiratory function decline rate in patients with advanced DMD. Long-term data from the DELPHI-Extension (DELPHI-E) study and SYROS (DELOS patients who transitioned to idebenone under an Expanded Access Program) are now presented. The aim was to assess the consistency of the long-term effect of idebenone on respiratory function across both placebo-controlled trials and their respective long-term data collections. 11 DELPHI-E and 18 SYROS patients with abnormal (<80%) forced vital capacity (as percent predicted, FVC%p) were treated with idebenone for an average of 2.0 and 4.2 years respectively. Annualized FVC%p decline rates were compared to untreated patients from SYROS or matched external controls (matched for baseline FVC%p) from the CINRG Duchenne Natural History Study (CINRG-DNHS). Mean (SD) baseline age was 13.6 (2.3) and 13.3 (2.7) years in DELPHI (*N*=11) and DELOS (*N*=18), respectively, and FVC%p was 47.2% (19.7%) and 58.7% (17.6%). For the first 2-year period, where data were available for both studies, the average annual decline rate was

comparable in treated patients (4.5% and 5.4% in DELPHI-E and SYROS) and lower than in untreated SYROS patients and external controls (7.9% untreated and 8.1% in CINRG-DNHS). During years 3 to 6, the annual decline rate was consistently lower than for matched controls. Treatment with idebenone resulted in a sustained reduction in the rate of decline in respiratory function across both placebo-controlled 52-week studies and across both long-term data collections, with follow-up time of up to 6 years. The consistency observed across 2 independent datasets adds to the robustness of the treatment effect of idebenone and its potential to modify the course of respiratory function decline in DMD.

Poster No. 104

A rare mutation in DYNC1H1 causing a mixed clinical phenotype of spinal muscular atrophy with lower extremity predominance and hereditary spastic paraplegia: a case series in a family

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Objective: To describe the identification of a rare mutation in the DYNC1H1 gene as a cause of a mixed clinical phenotype of spinal muscular atrophy with lower extremity predominance (SMA-LED) and hereditary spastic paraplegia (HSP).
Methods: Case series of three family members (father and two sons) across two generations.
Results: There was a history of early childhood-onset, progressive lower limb muscle weakness and atrophy. No relevant family history of neuromuscular disorders was reported on both the paternal and maternal sides of the family. Examination revealed markedly diminished tone and power in the lower limbs, with wasting and a positive crossed adductor reflex. There were no abnormalities detected in the upper limbs and sensation was preserved throughout. Neurophysiological testing showed moderate to severe chronic denervation of the lower limb muscles with sparing of the peripheral sensory nerves. HSP panel was negative but Charcot-Marie-Tooth (CMT) panel demonstrated a heterozygous sequence change in the DYNC1H1 gene: c.1808A>T p.(Glu603Val), which was present in all affected family members.
Discussion and conclusions: Mutations in the dynein gene are typically associated with SMA-LED or CMT. A mixed SMA-LED and HSP phenotype has previously been shown to be caused by mutations in BICD2. BICD2 encodes a golgin, which is a component of dynein-based transport, and plays a key role in mRNA transport during oogenesis and embryogenesis. We present the first case series of a mixed clinical phenotype of SMA-LED and HSP occurring due to a mutation in DYNC1H1. This was the first observation of the c.1808A>T p.(Glu603Val) variant at our laboratory and was not listed in the Genome Aggregation Database, suggesting an extremely rare variant.

Poster No. 105

Opening the lid on unilateral ptosis in paediatric NF1

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Introduction: Neurofibromatosis type 1 (NF1) is a genetic disorder with a birth incidence of 1 in 2–2700 individuals and prevalence of around 1 in 4000 worldwide. Ptosis is a well-documented feature in this condition and is known to be associated with plexiform neurofibromas or in the Noonan phenotype, with bilateral ptosis. Unilateral ptosis in the absence of a plexiform neurofibroma is not a common feature in NF1. We describe a number of patients with NF1 who demonstrated unilateral ptosis.
Methods: A retrospective cohort study was carried out using the patient database within the NF1 service based in St Mary's Hospital, Manchester, UK. Children and young adults aged 2 to 18 years with NF1 were identified via the patient database and patients with a presentation of ptosis were identified.
Results: Six children with unilateral ptosis were identified, four females and two males (ages 2–18, mean=9.5y). Five had unilateral ptosis affecting the right and one the left, with no differences observed between sporadic or familial disease. Five patients had complex disease; however, none had any other associated complication to account for the unilateral ptosis apart from NF1. They did not meet the diagnostic criteria for Noonan syndrome, and none had plexiform neurofibromas in the orbital or peri orbital area.
Discussion: It is unclear why there is an increased incidence of unilateral ptosis in our cohort of NF1 patients, in the absence of plexiform neurofibromas and Noonan's syndrome. Ptosis in NF1 has been associated with a Noonan syndrome phenotype in NF1 patients. The general hypotonia and myopathy observed in these patients could also factor into the causes for ptosis. Further research is necessary to investigate the aetiology of increased unilateral ptosis in NF1 patients.

Poster No. 106

Secondary outcomes of spinal surgery in patients with spinal muscular atrophy (SMA)

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Objective: SMA is a severe neuromuscular disorder characterised by progressive muscle atrophy and weakness. Scoliosis is a highly prevalent complication and surgery is almost invariably required in 'sitters'. Data on secondary outcomes are limited, and this study investigates post-surgical respiratory (FVC%) and motor function, weight gain, pain and satisfaction.

Methods: We retrospectively reviewed the notes of 33 patients who never walked or lost ambulation (SMA type II/III) who successfully underwent scoliosis surgery at Great Ormond Street Hospital: spinal fusion (25), magnetic (4) or traditional (4) growth rods. We performed phone interviews and run a focus group for families on pre and post-surgical satisfaction.

Results: Median follow-up before and after surgery was 3.9 (0.9–12.3) and 3.7 (0.4–10.5) years respectively. Mean annual rate of FVC% decline improved post-surgery in SMA II: –2.8 versus –7.4 (p<0.001), with similar trajectories in SMA III. Mean annual rate of Hammersmith Functional Motor Scale's scores decline did not change significantly (–1.2 vs –1.6, p<0.001), while the Revised Upper Limb Module's scores showed a less progressive deterioration (–1.3 vs –2.3, p=0.07). A negative deviation from previous weight curve after surgery was observed in 17/33 requiring food supplements (5); one/4 with significant weight loss (>5% of total weight) needed gastrostomy. Pain was frequently documented, especially hip pain (13/33) requiring painkillers (8), intra-articular steroids (2) and surgery (1). Nine/10 families participating in the phone interview reported major improvements in posture, physical appearance, self-image; all rated the procedure as very successful. However, 7/10 did not report significant improvements in quality of life due to reduced mobility and increased unmet care needs. Five families attended the focus group reporting on both positive and negative aspects of their experiences.

Conclusions: This study provides relevant data and suggestions to improve the current multidisciplinary approach of scoliosis surgery in children with SMA.

Poster No. 107

SUNFISH part 1: 18-month safety and exploratory outcomes of risdiplam (RG7916) treatment in patients with type 2 or 3 spinal muscular atrophy (SMA)

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Objective: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease caused by reduced levels of survival of motor neuron (SMN) protein due to deletions and/or mutations of the SMN1 gene. While SMN1 produces full-length SMN protein, a second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (RG7916/RO7034067) is an investigational, orally administered, centrally and peripherally distributed small molecule that modulates SMN2 pre-mRNA splicing to increase SMN protein levels.

SUNFISH (NCT02908685) is an ongoing, multicentre, double-blind, placebo-controlled study (randomised 2:1, risdiplam:placebo) in patients aged 2–25 years, with Type 2 or 3 SMA.

Methods: SUNFISH Part 1 (n=51) is a dose-finding study assessing the safety, tolerability and PK/PD of risdiplam; pivotal Part 2 (n=180) assesses the safety and efficacy of the risdiplam dose level that was selected based on results from Part 1. SUNFISH Part 1 included patients of broad age ranges and clinical characteristics (functional level, scoliosis and contractures). An interim analysis of Part 1 (data cut-off, 06 July 2018) showed a sustained, >2-fold increase in median SMN protein versus baseline after 1 year of treatment. Adverse events were mostly mild, resolved despite ongoing treatment and reflective of the underlying disease. Despite not being designed to detect efficacy, risdiplam improved motor function measures over 12 months versus natural history.

Results: Safety, tolerability and PK/PD will be reported from all patients in Part 1 who have received treatment with risdiplam for a minimum of 18 months. Updated Part 1 exploratory efficacy data, including motor outcome measures, will also be presented.

Conclusions: The clinical benefit of risdiplam is being assessed in Part 2, which is ongoing worldwide.

Poster No. 108

Intrafamilial phenotypical variability of autosomal recessive RYR1-related myopathy – a case report

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Objective: RYR1 encodes the skeletal muscle ryanodine receptor, an intracellular calcium-release channel that is crucial to excitation-contraction coupling in muscle. Gene variants can cause heterogeneous myopathies, including dominantly inherited central core disease. Both autosomal dominant (AD) and autosomal recessive (AR) pattern of inheritance have been reported.
Methods: Retrospective case notes review.
Results: Sibling 1: Female, presented during the first year of life with motor developmental delay. At 4 years of age she is able to sit unsupported and crawl but not stand or walk. She has facial weakness, but no feeding difficulties or ophthlamplegia. She has axial and proximal weakness with antigravity power in neck flexors and hip flexors (MRC 3/5) and sub-gravity power in hip abductors/extensors and knee flexors/extensors (MRC 2/5). There are severe hip, knee and ankle fixed contractures. Power and joint range is normal in upper limbs. Muscle biopsy showed type-1 fibre predominance and core-like structures.

Sibling 2: Female, presented at birth with feeding difficulties. At 3 months of age she is fully nasogastric fed. There is no facial weakness or ophthlamplegia. She has good head control with active head lift in prone, and antigravity power in hips, knees and ankles. She has mild hip and knee contractures and shoulder girdle weakness. Both siblings have been confirmed to be heterozygous for a RYR1 pathogenic frameshift variant (c.12063_12064dupCA p.(Met4022fs)) inherited from father and a likely pathogenic missense variant (c.14598G>C p.(Lys4866Asn)) inherited from mother. Both parents are asymptomatic.
Conclusions: The clinical and pathological features of AD RYR1-related myopathy are well recognized but much less is known about RYR1-related disorders secondary to an AR pattern of inheritance. We report two siblings with AR RYR1-related myopathy with similar genotypes but different phenotypic features demonstrating intra-familial variability and expanding current knowledge on this disorder.

Poster No. 109

Compound heterozygote mutations of the TiTiN gene in congenital myopathy of Irish siblings

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Introduction: We describe two cases of congenital myopathy associated with heterozygosity for three variants in the TTN Gene (TTN c.95076delC in combination with TTN c22226C>Tp. (Ser7409Leu) and TTN c.40405G >A p. (Asp13469Asn)).
Methods: Whole exome sequencing identified the compound heterozygote mutation.
Results: Our probands were the second and third children of consanguineous Irish parents who were fourth cousins. Antenatally, reduced fetal movements and amniotic fluid was noted with both probands. At birth, both had arthrogryposis and the second sibling required prolonged intubation at birth. Both had significant developmental delay; a more severe phenotype in the younger. On examination, both had myopathic facies, inability to bury eyelashes, full eye movements, high arches palates, drooling, a weak cry, micrognathia but a preserved suck. They both had long thin fingers, with thumbs held adducted and dimpling of elbows and hands. Peripheral reflexes were absent but there were good anti-gravity movements of the lower limbs. Both were noted to have pectus excavatum and progressive scoliosis. Muscle biopsies showed dystrophic features of fibrosis, hypertrophy and atrophy of fibres and variation in fibre size with increased fibrous connective tissue. Occasional central cords and multiple mini cords were also seen in the second proband. Whole Exome Sequencing identified the compound heterozygote mutation (TTN c.95076delC in combination with TTN c22226C>Tp. (Ser7409Leu) and TTN c.40405G >A p. (Asp13469Asn)).
Conclusions: Mutations in the TiTiN gene (TTN) have been implicated in several skeletal and or cardiac phenotypes to date. Each individual variant of the compound heterozygote has not been reported as pathogenic mutations and have been detected in the general population at 0.7% frequency. However, the presence of the triple count may certainly account for the severe phenotype of our probands.

Poster No. 110

Gene-replacement therapy (GRT) in spinal muscular atrophy type 1 (SMA1): long-term follow-up from the onasemnogene abeparvovec phase 1/2a clinical trial

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Objective: SMA1 is a rapidly progressing neurologic disease caused by biallelic survival motor neuron 1 gene (SMN1) deletion/mutation. The SMN GRT onasemnogene abeparvovec (formerly AVXS-101; approved in US) treats the genetic root cause of SMA and is designed for immediate, sustained SMN protein expression. In a phase 1/2a trial (START [CL-101]; NCT02122952), SMA1 patients received a one-time onasemnogene abeparvovec infusion at low dose (Cohort 1, n=3) or high dose (Cohort 2, n=12), and demonstrated improved outcomes versus natural history. No patients in

START received nusinersen during the 24-month follow-up after dosing. SMA1 patients in START could rollover into a long-term follow-up study (Study LT-001; NCT03421977). Primary objective: long-term safety.
Methods: SMA1 patients have annual visits (5y), then phone contact (additional 10y). Patient record transfers are requested. Safety assessments include medical history and record review, physical examination, clinical laboratory evaluation, and pulmonary assessments. Efficacy assessments include developmental milestone evaluation to determine maintenance of the highest achieved milestone in the parent study.
Results: As of 8 March 2019, 13 patients (Cohort 1, *n*=3; Cohort 2, *n*=10) had enrolled in Study LT-001 and had a baseline visit. For patients in Cohort 2, the mean (range) age and time since dosing were 3.9 (3.4–4.8) years and 3.7 (3.3–4.3) years, respectively. All patients in Cohort 2 (10/10) were alive. No developmental milestones achieved in START were lost, and new milestones have been achieved, supporting the durability of onasemnogene abeparvovec. Updated data will be presented.
Conclusions: One-time onasemnogene abeparvovec administration at the high dose continues to provide prolonged and durable efficacy with milestone development in LT-001.

Poster No. 111
MICU1-myopathy: a mitochondrial disorder that mimics a congenital muscular dystrophy – report of 2 siblings with variable phenotypes

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Objective: MICU1 encodes a selective calcium-channel subunit within mitochondrial inner membrane whose function is essential for buffering cytosolic Ca2+ transients and activating ATP production. Mutations in MICU1 have been reported in 20 different families with muscle weakness, fatigability and developmental delay, with normal lactate despite being a mitochondrial disorder and persistently elevated creatine kinase (CK) usually in the range of congenital muscular dystrophies (CMD). The phenotypic spectrum is highly variable and keeps expanding – other features include progressive extrapyramidal signs, learning disabilities, nystagmus and cataracts. We report the clinical features of 2 siblings from a consanguineous family with the homozygous c.1078–1G>C splicing mutation in MICU1.
Methods: Retrospective case notes review.
Results: Sibling 1: Boy, older sibling, presented aged 7 years. He had short stature which was investigated when found to have CK of 13 000IU/L. He complained of occasional cramps. Muscle biopsy showed mild dystrophic changes with reduced alpha-dystroglycan that indicated a possible congenital disorder of glycosylation. His MRI brain was normal. He was diagnosed with autism. Sibling 2: Girl, diagnosed antenatally with cerebellar hypoplasia, confirmed postnatally as inferior-vermis hypoplasia. Presented at 5 years with occasional cramps, mild tightness of tendo-Achilles, and CK of 3500IU/L. Her height and weight were on 2nd centile. Muscle MRI showed a small area of high signal in the left adductor magnus related to a group of normal vascular structures. Neurophysiology studies were normal. No other systemic involvement was seen in either of them. Next Generation Sequencing revealed the MICU1 mutation described.
Conclusions: Our work expands the phenotypical spectrum of MICU1 deficiency and highlights the variability in patients within the same family. Targeted analysis of the MICU1 gene in patients with high CK levels resembling a CMD picture may be warranted, even in the absence of prominent muscle features.

Poster No. 112
The role of dystrophin brain isoforms on early motor development and motor outcomes in young children with Duchenne muscular dystrophy

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Objective: Duchenne Muscular Dystrophy (DMD) is caused by DMD mutations leading to loss of the dystrophin protein. Half of patients have central nervous system (CNS) manifestations. Two dystrophin isoforms, Dp140 and Dp71, play an important role in CNS function. Those lacking Dp140 have a more severe CNS phenotype, most marked in those lacking Dp140 and Dp71. Our objective is to determine whether lack of Dp140 and Dp71 also has an adverse impact on early motor development.
Methods: The NorthStar Ambulatory Assessment (NSAA) is a scale of motor function. Clinical information for 320 DMD participants was classified by DMD mutation location and effects on isoform expression as follows: Dp140+_Dp71+ (Dp427 absent, Dp140/Dp71 present), Dp140-_Dp71+ (Dp427/Dp140 absent, Dp71 present) and Dp140-_Dp71- (Dp427/Dp140/Dp71 absent – all isoforms affected).
Results: Amongst 4 to 6 year olds, median total NSAA scores were lower in the Dp140-_Dp71+ (p=0.0088) and Dp140-_Dp71- groups (p=0.0001) than the Dp140+_Dp71+ group, most markedly in the Dp140-_Dp71- group. For example, for 6-year olds, median total NSAA scores were 26 (Dp140+_Dp71+), 23 (Dp140-_Dp71+) and 17 (Dp140-_Dp71-). Amongst 4 to 6 year olds, a lower percentage of participants achieved a full score of 2 (normal, achieves goal without assistance) for the NSAA sub-items in the Dp140-_Dp71+ (p<0.0001) and Dp140-_Dp71- (p<0.0001) groups than in the Dp140+_Dp71+ group, most markedly in the Dp140-_Dp71- group. For example, amongst 4-year-olds, percentage of visits for which a full score was recorded for jump were as follows: 56% (Dp140+_Dp71+), 19% (Dp140-_Dp71+) and 0% (Dp140-_Dp71-).
Conclusions: In addition to the known CNS phenotype, young DMD patients lacking Dp140 also exhibit lower median total NSAA scores and greater early motor delay, most markedly seen in those lacking both Dp140 and Dp71 (lacking all dystrophin brain isoforms). This has important implications for patient prognostication and clinical trial design.

Poster No. 113
Case report: lid hopping as a sign for atypical Miller Fisher Syndrome

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Background: Most commonly known as a rare subtype of Guillain-Barré, Miller Fisher syndrome (MFS) has evolved since it was first described in 1956. The syndrome is characterised by a triad of ophthalmoplegia, ataxia and areflexia but clinical variations do occur. It occurs more often in men than woman (ratio 2:1) with the average age of onset 43.6 years. MFS is associated with positive Anti GQ1b antibodies, which is concentrated in cranial nerves III, IV and VI – explaining the link with ophthalmoplegia.
Clinical case: We present an unusual case of a 2-year-old boy with background of macrocephaly and pre-existing developmental delay with a previous MRI which showed mild signal change in periventricular white matter bilaterally. He was admitted with a subacute history of proximal muscle weakness and fatiguability. He had no obvious focal neurological signs apart from intermittent lid hopping and ptosis. Differential diagnosis included myasthenia, demyelinating disorders or an underlying pre-existing luecodystrophy. Anti GQ1b antibodies were checked along with extensive metabolic investigations, lumbar puncture, muscle biopsy, anti-cholinesterase and anti-musk antibodies along with repeat MRI. All investigations were negative including MRI which showed no significant change from previous. The only findings were strongly positive anti GQ1B antibodies. In the interim, the patient was started on trial with Pyridostigmine with significant clinical improvement.
Conclusion: Atypical variants of MFS should be a differential in children with subtle eye signs without ophthalmoplegia. Lid hopping and fatiguability should raise the suspicion of MFS and anti GQ1b antibodies should be tested. Pyridostigmine has been reported to be effective in MFS.

Poster No. 114
Potential utility of muscle MRI in congenital myasthenia syndrome secondary to AGRN mutation found on whole exome sequencing (WES)

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Congenital myasthenia syndromes (CMS) are caused by genetic defects affecting neuromuscular transmission, resulting in muscle weakness and fatigability. AGRIN, an extracellular matrix molecule released by the nerve is essential at the neuromuscular junction. The large coding gene AGRN, has a number of exons and with increasing variants found on WES, it is time consuming and complex to undertake functional studies to define pathogencitiy. Previous reports of AGRN mutations have a phenotype with prominent distal leg weakness and changes in the soleus on MRI. We describe a differing presentation and striking changes on MRI, especially in the posterior compartment of the thigh. A 10-year-old presented with deterioration in his gait and difficulty climbing the stairs. He was born at term, via a normal vaginal delivery. His parents were consanguineous, and he had three well siblings. He was reported to walk by 2 years. On examination he had a waddling gait and was unable to run or hop. He had proximal weakness with a positive Gowers sign, together with weak eye closure. Muscle biopsy showed non-specific myopathic features, however an MRI of the lower leg found widespread fatty muscle atrophy of the thigh and calf with relative preservation of the adductor longus, rectus femoris and semitendonosis. WES revealed an AGRN mutation (c.5952_5963del) and a homozygous mutation in the nebulin gene (not felt to be clinically relevant). Single fibre EMG confirmed electrodecrement on repetitive nerve stimulation. The patient has been commenced on treatment with salbutamol. Our patient had very distinctive changes on MRI and non-specific muscle biopsy changes. Muscle MRI changes prompted further genetic testing when symptoms fitted a clinical diagnosis of a congenital myasthenic syndrome. With increasing variants found of unknown significance in these patients, collation of MRI imaging to try and elucidate patterns of changes will be important.

Poster No. 115
McArdle disease – no second wind phenomenon

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McArdle disease (glycogen storage disease type V) is an autosomal recessive condition caused by pathogenic mutations in both copies of the muscle glycogen phosphorylase (PYGM) gene encoding the muscle-specific isoform of glycogen phosphorylase, 'myophosphorylase' exclusively affecting skeletal muscle. It is the commonest form of glycogenosis. McArdle disease shows significant clinical variability, with symptoms ranging from mild discomfort during exercise to marked muscle weakness and rhabdomyolysis with myoglobinuria. The second wind phenomenon is unique to McArdle disease and consists of improved exercise tolerance with a decrease in heart rate after a rest. Despite the majority of patients recalling symptoms during the first years of life, McArdle is infrequently diagnosed in children, 66% of patients being diagnosed after 20 years of age according to a recent review. Here we report two patients diagnosed with McArdle disease at the age of 11 and 6 years respectively. Case one presented with fatigue and inability to increase pace of walking from the age of 4. Hills lead to earlier fatigue. She was able to participate in gymnastics and dancing. Presentation was with fluctuating CK levels (700 to 28 000). She had no second wind phenomenon or myoglobinuria. Case two presented at 6 years

with a history from 18 months of reduced exercise tolerance and myalgia after low intensity physical activity with no evidence of myoglobinuria or second wind. On formal assessment there was no evidence of muscle weakness or functional impairment. CK was persistently raised ranging from 650 to 4000. In the light of symptoms and CK levels a rhabdomyolysis panel was requested in both cases leading to diagnosis. Typical features of McArdle disease reported in adults were not present in either of our cases. It is important to consider the diagnosis in children with nonspecific features of myalgia, exercise intolerance and high CK.

Poster No. 116
Understanding anxiety experienced by boys with Duchenne muscular dystrophy: a qualitative focus group study

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Objectives: To explore characteristics of anxiety experienced by young males with Duchenne Muscular Dystrophy (DMD) using: 1. Qualitative analysis of focus group discussions with DMD boys and their parents. 2. Parent-report scales of anxiety/emotional problems.
Methods: Eight boys aged 7 to 18 years with DMD and 14 DMD parents participated in separate child and parent focus groups. Perspectives on anxiety were elicited using semi-structured discussions, and framework analysis was applied to identify themes. Scores on five parent-report scales were determined and scales were compared for content and sensitivity.
Results: From group discussions, six characteristics of anxiety were recurrently reported: catastrophic conclusions; rigidly held anxieties; extreme distress; unexpected/unfamiliar; social anxieties; physical changes and needs. Many features echo the anxiety phenotype in autism spectrum disorder (ASD). Four further themes described relevant contextual factors: Individual, Family, Social and Environmental responses. From parent-report scales, younger DMD boys (7–11y; n=12) had significantly higher Total, General and Social Anxiety scores compared to population means on at least two scales (p<0.01; p<0.01; p<0.05). The older DMD group (12–18y; n=6) trended towards higher scores in Total, General and Separation Anxiety (p=0.10; p=0.06; p=0.051) compared to population norms. Different scales varied in their diagnostic sensitivity and item content, which may influence their utility in DMD.
Conclusions: Anxiety can be a pervasive and impactful issue in DMD. It appears to have some shared traits with anxiety in ASD and may be influenced by situational factors, such as living with a disabling, life-limiting condition. Screening with standard anxiety scales may not accurately capture the full spectrum of the phenotype in DMD, therefore further evaluation to determine optimal screening instruments in DMD is warranted. However, multi-modal assessments tailored to DMD are key to identifying those in need of support to optimise the mental well-being of young people with DMD.

Poster No. 117
Evaluation of a tic management group for young people and their parents

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Objective: As part of the Clinical Psychology Service in Paediatric Neurology we developed a tic management group to support young people and their parents to develop positive coping in relation to their tics. The group combined psychoeducational, emotional regulation and Habit Reversal Therapy (HRT) components. This evaluation aimed to establish the effectiveness of these groups in reducing tics and associated distress.
Method: Twenty-eight children, aged 9 to 13 years and their parents attended one of seven tic management groups facilitated between February 2015 and November 2018. These children had been referred to the Clinical Psychology for support with tics.

Each group consisted of 5 weekly, 1-hour sessions with a review session 4 weeks later. A parent group was held in parallel. Both the young persons and parent groups were facilitated by the Clinical Psychology team. Homework tasks were provided to support HRT skill practice and consolidation of learning of the group content between sessions. The following pre and post group measures were completed by the young people and their parents: the Paediatric Index of Emotional Distress, the Yale Global Tic Severity Scale, the Parent Tic Questionnaire and Session Rating Scales. Measures were collated and descriptive data reviewed.
Results: 96% of children found the group was helpful in the management of tics. 57% of children were 'less bothered by their tics'. 70% of children felt more confident in controlling their tics. Parents reported a greater understanding of tics and a reduction in the severity of their child's tics.
Conclusions: Results indicate the tic management group is effective in building young peoples' understanding of tics, confidence in tic management whilst providing peer support. The findings also indicate that parents found the groups informative and valued the opportunity to share experiences with others.

Poster No. 118
Expectations of epilepsy surgery: a child and carer perspective

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Background: Patients with epilepsy often have deficits in cognitive, physical, psychological and social functioning, and treatment should aim to alleviate these deficits. Epilepsy surgery is considered for medication refractory epilepsy with aims to improve patient quality of life. A recent study highlighted the importance of a multidisciplinary workup prior to epileptic

surgery, including a neuropsychiatric assessment. Part of this assessment should identify patient expectations of epilepsy surgery, so that these can be addressed peri-operatively. At King's College Hospital (KCH), London, these assessments are routinely performed by the Paediatric Liaison Service as part of the Children's Epilepsy Surgery Service (CESS).

Aim: To analyse retrospective data of pre-operative patient and carer expectations between October 2018 – September 2019 at KCH.

Methods: A record of patient and carer expectations is routinely recorded as part of KCH CESS Neuropsychiatric assessments. The responses were compiled and analysed using qualitative content analysis.

Results: A preliminary survey of 12 cases with an average age of 11 (range 5–15) identified 15 responses that were grouped into broader classifications (cognitive, seizure experience, social process, school experience, mental state and general improvements). Simple analysis showed carers most often expected surgery to reduce the need for medications (42%), ablate seizures (33%), increase school performance (25%), independence (25%) and overall quality of life (25%). This compared to child responses, where the most common expectations were a reduction in lifestyle restrictions (42%), a cure for epilepsy (33%), decrease in medications (25%) and increased independence (25%).

Conclusion: Consideration of both child and carer expectations during pre-epilepsy surgery neuropsychiatric assessments is important in order for services to manage each individual's expectations. Unmanaged unrealistic expectations may lead to a negative psychological outcome for either child or carer. Expectations should be weighed up against an individual's clinical profile.

Poster No. 119

Neural correlates of conversion hemianaesthesia in an adolescent: a novel fMRI case study

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Aim: To highlight the novel functional Magnetic Resonance Imaging (fMRI) findings in an adolescent with rare conversion hemianaesthesia.

Methods: We hereby report a right-handed 14y old boy who presented with inability to perceive sensations on the right half of body without any motor weakness causing him to have frequent injuries on his right leg as well as burns on his right hand without realizing. When he wore a jacket, he felt warm on one side of the body more than the other. His birth and developmental history were non-contributory. Neurological examination was unremarkable except for right hemisensory disturbance. The MRI of brain and spine, peripheral nerve conduction studies and somatosensory evoked potentials did not show any evidence of dysfunction were normal. He underwent fMRI on a 3T Philips Achieva. The paradigm consisted of stimulating both the right and left hands and feet with three dissimilar stimuli (cold, brushing, pin-prick-pain). The order of the stimuli was pseudorandomised and after each stimuli delivery, feedback was obtained.

Results: Both the hand and foot sensory motor cortices were successfully stimulated. Irrespective of which hand was being stimulated, there was left hemisphere sensory motor cortex dominance (with the brushing and cold stimuli), however self-report from the participant confirmed detection of stimuli on the left-side only. There was more sensory-motor activation when the stimuli were delivered to the right hand. Pain stimuli successfully activated parts of the 'pain matrix', furthermore enhanced attention effects (frontal pole activations) were observed with right-sided stimulation (supports lack of stimuli detection ability). The pain stimuli were more effective on the hands than foot, reflected by increasing activation and also self-report from the participant.

Conclusions: The fMRI findings are unique and support the evidence of neuroplasticity and the current study paves the way for future studies investigating conversion hemianaesthesia.

Poster No. 120

Chronic paroxysmal hemicrania presenting as facial pain in a child with autism and bipolar disorder: diagnostic challenges

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Objective: We describe Chronic Paroxysmal Hemicrania (CPH), part of the Trigeminal Autonomic Cephalalgias (TAC's), in the context of Severe Learning Disability, Autism, Bipolar Disorder and Catatonia.

Case presentation: A boy diagnosed with disintegrative psychosis aged 3, revised to autism with bipolar disorder, had been on Carbamazepine with Risperidone for poor mood control. Withdrawal of Risperidone produced Tardive Oromotor Diskinesia responsive to Clonidine. Aged 11, when mood improved on Aripiprazole, Carbamazepine was withdrawn. He then presented with episodes of distress preceded by withdrawal, unilateral but not side-locked facial flushing, with additional flushing of neck, back and wrists. Behaviours included hitting wrists off walls, chewing of hard objects and requesting pressure to his head. Episodes occurred 8–9 times/day, lasting 2–60 minutes. He showed rhinorrhea and tearing, attributed to crying, during events. The attacks self-terminated.

Results: MRI and electroencephalogram were normal. Failed pharmacological trials included Paracetamol, Amitriptyline, Gabapentin and Oxcarbazepine. Diclofenac provided mild pain relief and Morphine reduced the incidence of attacks. Reintroduction of Carbamazepine resulted in improvement at 30mg/kg/day but did not eliminate pain. Sequencing of SCN9a was normal. A plan to wean morphine alongside a trial of Indometacin, initially at 25mg twice-daily was successful at 50mg twice-daily. Episodes ceased, including all autonomic features. Exacerbation at 4 weeks occurred in context

of an intercurrent illness and was managed with an additional dose of Indometacin.
Conclusions: CPH is underreported in the paediatric age group. In our case, the patient's inability to describe events, and an additional psychiatric diagnosis added complexity. The possibility of pain as a cause for early psychotic breakdown in a developmentally vulnerable child cannot be excluded. Criteria emphasising side-locked headache and autonomic features, and not recognising associated symptoms elsewhere may also delay recognition in children.

Poster No. 121
Diagnosis and management of paediatric idiopathic intracranial hypertension (pIIH): identifying areas of uncertainty in clinical practice

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Objectives: pIIH can be a challenging condition to diagnose and manage with risks of misdiagnosis, permanent sight loss and frequent comorbidities. We aimed to review our practice to identify areas of uncertainty to help formulate important questions to address within a clinical guideline.
Methods: A single centre retrospective case notes review of all cases referred to Neurology with suspected pIIH (papilloedema confirmed by a consultant ophthalmologist in all cases) during an 18-month period.
Results: 14 (12F: 2M) cases were identified. Age range 8 to 15 years. Mean 13 years. 8/12 had a BMI >98th centile. One case was referred to an obesity service. 6/14 had a comorbid headache disorder and 4/14 had anxiety/depression. All cases had neuroimaging (13 MRI, 1 CT) with 4/14 having dedicated venography. In 2/14 cases Lumbar Punctures (LP) were conducted under General Anaesthesia (GA). In 4/14 cases LP was not done; 2 due to presence of a Chiari malformation and 2 due to procedural failure related to body habitus. Intracranial pressure (ICP) monitoring was done in one of these four cases. All children were treated with acetazolamide as first line therapy. Frusemide, zonisamide and topiramate were also used in single cases. 5/14 children had repeat LPs due to failure of resolution of symptoms. 2/14 cases had sight threatening pIIH with permanent visual loss in one case. 5/14 cases were discussed with Neurosurgery. One child with evolving visual failure had an emergency Ventriculo-Peritoneal shunt.
Conclusions: Important questions raised were: Should all obese children with pIIH have access to a specialised obesity service? Should all children have dedicated venographic imaging? How reliable is measuring CSF opening pressure under GA?

Where LP is not possible should ICP monitoring always be done? Should repeat LPs be done for persistent symptoms? Should CSF diversion surgery be restricted to cases of sight threatening pIIH only?

Poster No. 122
A case of Revesz syndrome in a 5 month old infant

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Objective: To describe a case of Revesz syndrome due to a de novo missense variant in TINF2.
Case report: A male infant was born at 35 weeks gestation by emergency LSCS due to maternal hypertension and reduced amniotic fluid. From 32 week's gestation, reduced fetal growth was identified. The proband was born by at 35 weeks. Birth weight was 1.7kg (0.4th–2nd centile) and occipitofrontal circumference (OFC) was 31.7cm (2nd- 9th centile). He spent 15 days in the SCBU. He developed thrombocytopenia (nadir: 67×109/L), which resolved pre-discharge. Periventricular calcifications on cranial ultrasound prompted TORCH screen and ophthalmology review. A right pre-retinal haemorrhage with overlying organised vitreous haemorrhage was identified, which remained stable on subsequent reviews. Aged 8 weeks, he was smiling, fixing and following with good head control. Aged 5 months, he developed new wobbly eye movements and was no longer fixing or following. Bilateral retinal detachments were identified. CT and subsequent MRI showed diffuse calcification within the thalami, posterior limb of the internal capsule, deep white matter, cerebellar atrophy and thin corpus callosum. Findings on examination included OFC of 0.4th centile, rotatory nystagmus and central hypotonia. Whole-exome sequencing identified a pathogenic de novo variant in TINF2 (c.845G>A, p.Arg282His). He subsequently developed thrombocytopenia and anaemia and is transfusion dependent.
Discussion: TRF1 interacting nuclear factor-2 (TINF2), protein regulates telomerase and prevents telomere shortening. Revesz syndrome is a severe form of Dyskeratosis Congentia, with multi-system involvement and early onset in-utero. Revesz syndrome is characterised by intrauterine growth retardation (IUGR), microcephaly, cerebellar hypoplasia, bilateral exudative retinopathy, intracranial calcifications and progressive bone marrow failure. Revesz syndrome is distinguished from Hoyeraal-Hreidarsson syndrome by the presence of retinopathy. Telomere disorders should be considered in infants with a background of IUGR, thrombocytopenia, retinopathy and intra-cranial calcifications with a negative TORCH screen, as early features mimic congenital infection.

Poster No. 123

Reversible cerebral vasoconstriction syndrome in sickle cell anaemia: a case report

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Objective: Currently the most commonly reported neurological complication of SCA is overt stroke. Reversible cerebral vasoconstriction syndrome may be more frequent in patients with Sickle cell anaemia than reported at present. The scarcity of prevalence studies however makes it difficult to improve diagnostic accuracy in these patients.
Methods: A 16-year-old Ghanaian female was rushed to the paediatric emergency room with first episode of sudden severe global headaches initially started 8 hours prior to arrival. The headache was so excruciating that she described it as her heart was beating in her head. There was associated neck pain, back pain, dizziness, and vomiting. There was no fever or dark urine. She was first diagnosed with Sickle cell anaemia (genotype SS) at 2 years of age after she was treated for dactilitis. She had since then been in her usual state of health with no history of blood transfusions or surgeries or admissions. She was compliant with her medications (Folic acid 5 mg daily). A physical examination and all investigations were also normal. On day six of admission patient had a generalized tonic clonic seizure with some degree of left sided weakness after having her bath. This was aborted with intravenous diazepam and a magnetic resonance imaging (MRI) of the brain was requested. The MRI of the brain revealed diffuse narrowing of the cerebral arteries with no areas of bleeding or oedema. Reversible Cerebral Vasoconstriction Syndrome was therefore suspected.
Results: The headache rapidly improved after starting Nimodipine and repeat angiography at 3 months showed no vasoconstriction, confirming the diagnosis.

On follow up she is doing well academically with no neurological deficits.
Conclusions: The true incidence of RCVS in patients with Sickle cell is uncertain, thus sensitizing medical practitioners is important.

Poster No. 124

Status dystonicus: is it a gut feeling?

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Introduction: Status dystonicus (SD) is a life-threatening disorder of generalised, painful dystonic movements and muscular spasm in patients with severe neurodisability. While rare, it may be complicated by rhabdomyolysis, multi-organ dysfunction, and death. Infection, pain, GORD, and medication failure are common triggers, but in approximately one-third of cases, SD is idiopathic. Mordekar et al. (2017) identified a series of 11 patients in whom SD occurred secondary to GI dysfunction. Assisted feeding (e.g., via gastrostomy), and aberrant bowel peristalsis may trigger the onset of SD. This was a retrospective analysis which aimed to estimate an incidence rate for feed-induced SD (FISD).
Methods: Patients presenting to Sheffield Children's Hospital over a 5-year period with SD were identified. Episodes were studied to assess for the nature of the onset of SD and as to the likelihood that the trigger was feed related. Incidence of FISD as a proportion of total SD was calculated and OR calculation performed to explore relative risk of SD between individual trigger factors.
Results: Twenty-four individual episodes of SD were identified. 13 (54%) arose from non-feed-related sources (nFISD), and 11 were felt to be FISD (46%). 6 additional patients were entered into a feed-induced dystonia (FID) group, whom showed clinical evidence of dystonia in relation to GI sources, but not SD. With the exception of infection, the relative risk of SD secondary to GI dysfunction was significantly higher than pain/GORD and medication failure combined (OR 0.11 (95% CI 0.02–0.56) and 0.05 (95% CI 0.01–0.44) respectively).
Conclusion: GI dysfunction coupled with severe neurodisability could serve as a trigger in a number of previously idiopathic SD cases through disruption of the neuro-enteric axis. However, overlap between triggers for FISD and nFISD, and significant variation between groups is evident, in addition to a lack of statistical study power. Large, prospective studies are needed in the future to corroborate with these findings.

Poster No. 125

Dystonia can twist the patient, physician and the scans: hypermanganesemia, a rare cause of dystonia in children

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Introduction: Manganese (Mn) is a chemical element with symbol Mn and atomic number 25. Mn in the environment can cause toxicity with dystonia and other movement disorders. Waterborne Mn has a greater bioavailability than dietary manganese. According to results from a 2010 study, higher levels of exposure to Mn in drinking water are associated with increased intellectual impairment and reduced intelligence quotients in school-age children. We have recently reported a suspected autosomal recessively inherited syndrome of hepatic cirrhosis, dystonia, polycythemia, and hypermanganesemia in cases without environmental Mn exposure. The rarity of the disease can become a challenge for the physicians to recognize this as a cause of dystonia in children. It also has a characteristic finding on MRI with T1 hyperintensity in basal ganglia rather than on T2.
Case report: We present a case of a 6-year-old girl with dystonia who was previously healthy. She has been suffering from this for the last 6 months and currently one of her 4 years old sister started showing similar symptoms. Physical examination revealed marked dystonia (score of 24 on Baryalbright dystonia scale) and polycythemia (Haematocrit 65). Magnetic resonance imaging (MRI) brain showed basal ganglia hyperintensity on T1 weighted images. Hypermanganesemia

was suspected and samples send for serum level which came out to be high. Water samples were tested, which came out to be normal. Chelation was done and the dystonia improved.
Conclusions: Dystonia in children should be thoroughly investigated and rare, treatable causes should not be ignored.

Poster No. 126

Withdrawn.

Poster No. 127
The use of sodium valproate in girls in the South Eastern Trust, Northern Ireland: 2018 audit

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Objectives: Sodium valproate is used primarily for the treatment of epilepsy in children. It is a well-established teratogen, with 4 in 10 babies at risk of developmental disorders and 1 in 10 babies at risk of birth defects. This risk has been known since the 1970s and yet it is estimated that since then 20 000 children in the UK have been left with disabilities as a result. In 2016, the Medicines and Healthcare Products Regulatory Agency released guidance for its use, which included a risk acknowledgement form. Patient safety alerts were issued in 2017 asking all organisations to identify females taking this medication. We aimed to identify all girls taking sodium valproate in the South Eastern Trust under paediatrics requiring annual risk assessment; patients under the additional care of a neurologist; patients receiving an annual review.
Methods: Patients were identified through paediatric epilepsy nurse records and data collected through the electronic care record and medical notes from August 2018 to December 2018.
Results: 24% (n=30) of girls with epilepsy currently taking sodium valproate, 73% under the age of 10 years, 37% profound learning difficulties/disability and considered to be at low risk of pregnancy, 7% (n=2) potentially currently at risk, 81% were under the additional care of a neurologist, 87% reviewed in the past year.
Conclusions: Sodium valproate must not be considered first line treatment in girls with epilepsy and >75% of girls in our trust are not receiving it. Of those receiving it, the majority are felt to be low risk due to young age and/or profound disability. We identified two patients at risk and steps were taken to ameliorate this. We have demonstrated good awareness; however lifelong education of families is crucial to reducing the burden of fetal valproate syndrome.

Poster No. 128
Rett syndrome as a movement and motor disorder – a narrative review

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Rett syndrome (RTT) is neurodevelopmental disorder affecting approximately 1 in 10 000–15 000 live female births, most commonly associated with mutations in the MECP2 gene. Hand stereotypies and gait disturbance, as well as spasticity and dystonia, have been noted in RTT since the first descriptions of the syndrome.
Objective: This review aimed to explore the prevalence of reported movement disorders in RTT. Data sources and extraction: Pubmed and Embase databases for papers describing features of movement disorders in Rett Syndrome. Papers were selected for inclusion to be reviewed if they included description of case report, cohort or case-series of patients with RTT which included a description of clinical features of their movement disorder. Selected papers were divided into 3 epochs: (i) pre-1999, (ii) 2000 to 2009, and (iii) 2010 onwards.
Results: 32 studies (13 in the first epoch, 10 in the second epoch and 9 in the third epoch) reported on movement disorders including stereotypies in RTT patients. Hand stereotypies were almost universal in reported cases, diminishing but not disappearing over time. Gait disturbance and ataxia/tremor were also very common (>50% cases). Elements of hypertonia were also common, increasing with age. In earlier descriptions spasticity was commonly described, with more frequent reference to dystonia/rigidity in more recent reports. Myoclonus and choreoathetosis are uncommonly reported in RTT.
Conclusions: Movement disorders beyond hand stereotypies are common in RTT, most notably tremor. Hypertonia is a common feature seen in RTT, increasing in prevalence with age, and with an apparent change in nomenclature over time, (i.e., early epoch spasticity, late epoch dystonia). Dystonia was specifically reported in 229/417 cases. Further work is required to explore the relative contribution of dystonia and rigidity to hypertonia in RTT, as well as the impact of these impairments when present.

Poster No. 129
Study of clinical spectrum and disability assessment of childhood migraine

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Introduction: Headache is the common complaint in children, and the source of it, a great deal of worry for general practitioners and parents. One of the commonest causes of headache in paediatrics is migraine.
Methods: A prospective study was conducted to evaluate the demographic data, clinical spectrum and grading the child

with migraine by using the Paediatrics Migraine disability Assessment (Ped-MIDAS) questionnaire and to start prophylactic treatment for those with the higher grades in the department of paediatrics in tertiary care hospital. All children with migraine from age 5 to 18 years were included while all other types of headache cases were excluded.
Results: Total 112 children with migraine were studied. Approximately 80% children complained of bilateral frontotemporal headache in which 69.64% presented with throbbing type. Other associated features were photophobia, phonophobia, nausea and vomiting. 75% had skipped meal, followed by altered sleep and exam stress as aggravating factors. 94.6% required medication for headache relief. Headache duration and frequency was approx. 17 days and 9 days/month. 57.1% cases were diagnosed migraine without aura and 42.9% cases were diagnosed as migraine with aura. Loss of full school days due to headache was approx. 2 days for period of 3 months. Based on Ped-MIDAS score, 50% of children with migraine had grade I disability while 42.9% and 7.10% cases had grade II and grade III disability respectively. Correlation of Ped-MIDAS score with frequency and severity were significant ($p<0.001$) while with duration of headache was insignificant ($p<0.245$).
Conclusions: All patients with higher Ped-MIDAS grade are warranted prophylactic treatment. Both Ped-MIDAS scores and grading can be successfully used for assessing the migraine disability and its easier, less time consuming, bedside diagnostic tool, can be used widely in routine clinical evaluation and management.

Poster No. 130
The differential diagnosis of variant Creutzfeldt-Jakob disease in UK children 1997 to 2019

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Objective: To review the cases referred to this UK-wide study of children with possible variant Creutzfeldt-Jakob disease (vCJD) and report the differential diagnosis in children presenting age 10 years or older.
Methods: Children meeting the case definition for progressive intellectual and neurological deterioration (PIND) were identified via the British Paediatric Surveillance Unit. Details were obtained by standard questionnaire.
Results: Between April 1997 and August 2019, 4589 children had been notified to the study. 2068 were found not to meet the PIND case definition. 2006 had an underlying diagnosis to explain their deterioration, with over 210 different disorders including 6 vCJD cases (the last identified in 2000). There were 104 children who presented to clinicians when aged 10 years or over, including all the 6 vCJD cases. Of the other disorders in this age group the commonest were: mitochondrial cytopathy 16, adrenoleukodystrophy 9, Lafora body disease 8, Huntington's disease 7, neuronal-ceroid lipofuscinoses 6, Niemann-Pick type C 6, metachromatic leukodystrophy 4, SSPE 4, Wilson's disease 4. When reviewed in 2017 there was no underlying diagnosis in 225 PIND cases; 108 of them had died – only 14 underwent autopsy.
Conclusions: The recent identification of the first patient with vCJD who was MV heterozygous at PRNP codon 129 reinforces the need for continued vCJD surveillance, particularly as a study of archived appendix samples from UK hospitals published in 2013 indicated that approximately 1 in 2000 of the UK population is carrying abnormal prion protein in the gastrointestinal tract. In the absence of a validated vCJD screening test the PIND Study remains the only means of performing systematic surveillance of the neurodegenerative diseases that make up the differential diagnosis of vCJD.

Poster No. 131
Children with progressive intellectual and neurological deterioration in Northern Ireland 1997 to 2019

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Objective: To review referral patterns, diagnoses and outcome of children referred to this UK-wide study and compare Northern Ireland (NI) cases with UK cases.
Methods: Children meeting the case definition for progressive intellectual and neurological deterioration (PIND) were identified via the British Paediatric Surveillance Unit. Details were obtained by standard questionnaire.
Results: NI children: between April 1997 and July 2019 there were 93 notifications. Numbers notified each year: range 1 to 14, median 3. Source of notifications: general paediatricians 46, paediatric neurologists 27, community paediatricians 13, others: 7. Of the 50/93 cases meeting PIND criteria 38 had an underlying diagnosis, 6 had no diagnosis, 6 were under review. There were 22 different disorders in the 38 diagnosed children. The 5 commonest diagnostic groups were: white matter disorders 10, neuronal ceroid lipofuscinoses 7, mucopolysaccharidoses 4, GM2 gangliosidoses 4, mitochondrial disorders 2. No child with variant Creutzfeldt-Jakob disease (vCJD) was identified. Of 6 children with undiagnosed PIND, 4 were known to have died, one underwent autopsy. All UK children: by August 2019 4589 children had been notified, 2068 not meeting PIND criteria. 2006 had an underlying diagnosis, with over 210 different disorders including 6 vCJD cases (the last identified in 2000). The commonest diagnostic groups were similar to NI cases. 225 PIND cases had no underlying diagnosis; 108 of them had died – only 14 underwent autopsy (reviewed in 2017).
Conclusions: PIND surveillance in NI is proceeding well; notifications come from a range of paediatricians. NI findings are similar to the whole UK but no vCJD cases have been identified in NI children. However, the risk remains so we hope that NI paediatricians will continue to notify children with PIND.

Poster No. 132

Expressive dysphasia due to reversible splenial lesion syndrome (RESLES): a case series

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Objective: Transient lesions in the splenium of corpus callosum (SCC) are rare findings in MRI brain in paediatrics. In literature, it has been described as Reversible Splenial Lesions Syndrome (RESLES) and Mild Encephalitis/Encephalopathy with Reversible Splenial Lesions (MERS). The condition has diverse aetiology and widely variable neurological presentation but the prognosis is usually favourable. We present two cases of RESLES with predominantly expressive dysphasia but varying causal associations.

Method: Retrospective review of RESLES case series exploring clinical course, investigations, neuroimaging, treatment and recovery.

Result: Case 1: A 15 year-old-girl presented with confusion, fever and low oxygen saturation. She had Alagille syndrome and partially corrected Tetralogy of Fallot. Her neurological manifestations were expressive dysphasia, dysarthria and difficulties with spatial awareness. Interestingly she was able to use occasional words that were abusive in nature. MRI showed prominent focus of abnormal signal and restricted diffusion in SCC. Her blood culture grew Staphylococcus Aureus and Echo revealed infected shunt. Treatment involved shunt replacement and prolonged IV antibiotics. Repeat MRI showed resolution of splenial lesions. She continued to improve neurologically. Case 2: A 9 year-old-girl presented with paroxysmal episodes of head turning, head drop and staring for a few seconds. She refused to feed. She showed emotional lability with expressive dysphasia but preservation of expletives. Neurologically she was intact. MRI brain showed high signal with restricted diffusion in SCC. Her blood and CSF investigations including MOG, Aquaporin, NMDAR, Lyme antibodies were negative except ASOT was 400. Her EEG was normal. She received a course of IVIg and Azithromycin. Her repeat MRI showed resolution of the lesion in splenium. She made complete recovery over next few months.

Conclusion: Splenial lesions are rare but clinically significant but not 'Non-Specific'. Expressive dysphasia is a prominent symptom. Awareness of RESLES/MERS will avoid unnecessary investigations and assist in the prognostication.

Poster No. 133

Management and outcome of paediatric headaches in a tertiary paediatric neurology setting

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Background: The evidence-base on managing paediatric-headaches is sparse resulting in wide variation in practice with NICE guidelines commencing over 12 years of age. This study aims to evaluate outpatient management of Paediatric headaches.

Objective: To investigate paediatric headache referrals to a tertiary hospital over a 1-year period, exploring patient demographics, headache type, role of neuroimaging, management and outcome.

Methods: This prospective study reviewed headache referrals for the year 2018–2019. The data was collected following weekly emails to relevant clinicians. The patient demographics, headache classification, imaging, management and outcome were collated on a proforma from the electronic patient-records.

Results: There were 99 patients. The median age of patients at first outpatient appointment was 12 years (range 3–17y); 63.6% were female. Incidence of headaches increased with age. Female preponderance of headaches existed in all age groups and was most substantial post-puberty with a 2.4:1 female-to-male ratio in patients aged 13 to 17 years. Migraine was the most common diagnosis, affecting 46.5% of patients. 51% of referred patients underwent a brain MRI scan, all of whom had a normal neurological examination. No MRI scans found pathology contributing to headache presentation. 91% of patients were discharged from neurology clinic after first or second neurology appointment. Non-pharmacological management was the most common intervention and consisted of: headache diary, lifestyle advice, education, relaxation techniques. The most common medications prescribed bar simple analgesia were sumatriptan (12%), propranolol (9%) and pizotifen (9%).

Conclusions: A multidisciplinary and biopsychosocial approach to managing paediatric headaches, consisting of non-pharmacological and pharmacological *Methods* resulted in a positive outcome, with majority discharged from tertiary care after first appointment. Prescription of sumatriptan and propranolol first line for acute and prophylactic management respectively, was in accordance with current clinical recommendations. The role of MRI scanning for paediatric headaches requires further exploration and perhaps more stringent guidelines.

Poster No. 134

A comparison of the active standing test (AST) and head-up tilt test (HUTT) in children and young people

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Objective: The Head-Up Tilt Test (HUTT) is the gold standard autonomic function test for identifying disorders of Blood Pressure (BP) and Heart Rate (HR) regulation, specifically with excessive falls in BP and or HR, as well as excessive postural tachycardia (PT). The 10 minute Active Standing Test (AST) is quicker and easier to apply, e.g., in an outpatient clinic, and may be more sensitive in demonstrating PT. We aimed to compare the yield of these abnormalities when using AST vs HUTT.

Methods: This was a retrospective, clinical notes review, and registered clinical audit of unselected consecutive children and young people undergoing HUTT immediately preceded by an AST.
Results: Data was available on 86 children and young people, 56 (67%) female, aged 3 to 18 years (median 14). 12/84 (14%) with complete data sets for the first 10 minutes of HUTT and the AST had abnormally large drops in BP and or HR on HUTT. Only 1/12 positive on HUTT was also positive on AST. However, an additional 6/84 (7%) were positive on AST but not on HUTT, giving 18/84 (21%) positive in total. 8/86 (9%) with HR data sets for 10 minute HUTT and AST had abnormally large rises in HR on HUTT. Only 3/8 positive on HUTT were also positive on AST. However, an additional 10/86 (12%) were positive on AST but not on HUTT, giving 18/86 (21%) positive in total. While HUTT yielded more cases with significant falls in BP and or HR than AST (14% vs 8%), combining the tests gave the highest yield (21%). While AST yielded more cases with significant rises in HR than HUTT (15% vs 9%), combining the tests gave the highest yield (21%).
Conclusions: We recommend routinely undertaking a 10 minute AST prior to the 45 minute 60° HUTT, in children and young people.

Poster No. 135
Respiratory function in SMA type 2 and non-ambulant SMA type 3: longitudinal data from the international SMA consortium (iSMAc)

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Objective: The aim of our work is to describe the respiratory function trajectories and their correlation with motor function in a cohort of Spinal muscular atrophy type 2 and non-ambulant SMA3 paediatric patients.
Methods: This is a retrospective 9-year study in patients recruited in the iSMAc natural history study (UK, Italy, US). The following respiratory data were collected: lung function data (Forced vital capacity absolute (FVC) and FVC% predicted, Non-Invasive ventilation (NIV) requirement. Recumbent or ulnar length were used as surrogate for height in FVC%pred. calculation. Comorbidities affecting lung function such as aspiration were collected. Anthropometrics and motor function scores as Hammersmith functional motor scale (HFMS), Revised performance of upper limb (RULM) were noted. We excluded patients in interventional clinical trials and Nusinersen therapy.
Results: Data were available for 437 patients: 348 SMA2, 89 SMA3. Mean age at first visit was 6.9 (±4.4) and 11.1 (±4) years for SMA2 and 3. 180/215 (84%) SMA2 and 39/49 (80%) SMA3 had scoliosis. 85/236 (36%) SMA2 and 1/62 (2%) had swallowing impairment. Yearly rate of progression of FVC% predicted (available in n=260) was 3.6% in SMA2 and 3.5% in SMA3. In SMA2, FVC% predicted declined steeply from 5 to 15 years of age, followed by a levelling. Conversely, in SMA3 patients FVC% predicted declined slower but steadily from 10 years of age. 136/298 (46%) SMA2 and 8/71 (11%) required non-invasive ventilation due to respiratory infections or hypoventilation. In SMA2 FVC% predicted positively correlated with HFMS and RULM (r=0.67, p<0.001; r=0.61, p<0.001) as in SMA3 (r=0.67, p<0.001; r=0.61, p<0.01).
Conclusions: The results of this ongoing collaborative work suggests that in SMA2 and 3 lung function declines from age 5 and 10 respectively. Lung and motor function correlate well in both SMA2 and 3. This data will help the assessment of the long-term efficacy of new treatments for SMA.

Poster No. 136
Prospective review of brain magnetic resonance imaging referrals in children 12 years or over following guideline implementation changes

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Objective: NICE guideline CG150 on headaches in children over 12 years old sets standards for neuroimaging but concern over inappropriate requests remain (cf.10.1136/archdischild-2019-rcpch.177). This review aims to study the appropriateness of MRI brain referrals following implementation of local changes to improve compliance to the NICE CG150 standard.
Methods: Following an earlier survey (ES; 01/06/16 – 30/06/17) of MRI brain referrals for headaches in children over 12 years, key recommendations included adding pop-ups in the neuroimaging request system (ICE) of NICE CG150 and Headsmart clinical guideline V2 as well as verbal consent obtained from senior paediatrician before request was made. Following these implementations, requests for MRI brain were analysed during 01/06/2018 – 31/12/2018 in the same District General Hospital. Referral was deemed compliant if the NICE guideline CG150 standard were met.
Results: 50 children were referred for MRI brain scan (mean 7/month vs 10/month in ES). 43 (86%) referrals were compliant (vs 67% compliance in ES). 13 (26%) referrals were 'urgent' (vs 30% urgent ES) and 37 (74%) 'routine' or non-urgent (vs 68% routine ES). 12 (92%) of urgent referrals (vs 35% ES) and 31 (84%) of routine referrals (vs 65% ES) were compliant. Urgent scans were done average 3.3 days (vs 4d ES) and routine scan average 16.3 days (vs 14d ES). MRI scan on 3 (23%) children with urgent referral (vs 87% ES) and 2 (0.05%) on routine referral (vs 0% ES) showed a significant brain lesion. Benign findings reported on MRI brain scans were cysts (i.e., pineal, arachnoid), arteriovenous malformation, mild ventricular dilatation.
Conclusions: Compliance to NICE guideline increased by 28% and frequency of referrals have reduced since the above implementations. Urgent referrals are found to have high likelihood

of significant lesions. A review of practice of asking routine or non-urgent MRI requests should be considered in view of an unlikely significant result.

Poster No. 137

Retrospective review of brain magnetic resonance imaging referrals in children less than 12 years

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Objective: MRI brain guidelines for neuroimaging in less than 12 years exist (Headsmart clinical guideline V2 and NICE Epilepsy QS27) but are limited. This study aimed to assess current practice of MRI brain referrals in children under 12 years.
Methods: Retrospective review of MRI brain referrals in children under 12 years performed between 01/01/2018 – 31/12/2018 in a District General Hospital. Referrals were grouped under 3 categories: Headsmart clinical guideline V2, NICE Epilepsy QS27 and Miscellaneous (including children with global developmental delay, neurological deficit, sensorineural deafness, sepsis, preterm, craniosynostosis, trauma, endocrine, Non accidental injury).
Results: 215 MRI brain scans were done (M:F 1.1:1); 113 (53%) done under 5 years with 33 (15%) in first year and average of 18 per year thereafter. 69 (32%) were urgent requests and completed in mean 6.7 days (range 0–16d). 146 (68%) were non-urgent requests and completed in mean 50 days (1–120d). 92 (43%) referrals under Headsmart and 33 (36%) of these were urgent requests; significant brain abnormality was seen in 26 (79%) in urgent and 1 (0.01%) in non-urgent cases. 45 (21%) referrals under Epilepsy QS27 and 12 (27%) were urgent requests; significant brain abnormality in 2 (17%) in urgent and 2 (6%) in non-urgent cases. 78 (36%) were Miscellaneous requests and 24 (31%) were urgent; significant brain abnormality in 8 (33%) in urgent and 13 (24%) in non-urgent cases. Overall MRI brain showed significant abnormality in urgent requests (52%) compared to non-urgent requests (11%). Benign findings reported on MRI brain scans were cysts (i.e., pineal, arachnoid), arteriovenous malformation, mild ventricular dilatation.
Conclusions: Most MRI brain referrals are done in 0 to 5 years age group. Urgent referrals following Headsmart and Epilepsy QS27 guidelines more likely appeared to identify significant brain abnormality. Clinicians seem to prioritise their patients well. Guidelines for Miscellaneous conditions may help keeping the referrals more robust.

Poster No. 138

Assessing the role of ketogenic dietary therapy in ring chromosome 20 syndrome: a patient led approach

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Objective: Ring Chromosome 20 Syndrome (r[20]) is an ultra-rare disease characterised by drug-refractory epilepsy, cognitive impairment and behavioural problems. Non-pharmacological treatments should be considered alongside antiepileptic drugs (AEDs) early after diagnosis to benefit prompt seizure control and preserve cognitive function. We aimed to understand the use and experience of Ketogenic Diet Therapy (KDT) in r(20) by Patients Families Carers (PFCs) and Healthcare Professionals (HCPs), assessing its efficacy and safety, and contrasting NHS KDT service provision with patient demand.
Methods: Literature searches were conducted on use of KDT in r(20) and similar complex epilepsies. Two surveys were developed to gather demographic, diagnostic and clinical care information. Surveys were qualitative and descriptive with patient and expert collaborators assessing content accuracy and readability. Responses were discussed at a patient and expert workshop.
Results: The number of responses (42 PFCs, 23 HCPs) was considered significant given the ultra-rare status of r(20). 50% of PFCs had tried KDT. Seizure activity, behaviour and cognitive outcomes were ranked equally important by HCPs and PFCs. Significant improvement in seizure activity, cognition and alertness were reported; side-effects were typically mild but with one report of increased seizure frequency. The high rate of comorbidities, older age at presentation, behavioural problems and cognitive impairment can make implementing KDT in r(20) challenging. PFCs report quality of life would be most improved with reduced AED side-effects; HCPs report they would consider reducing or withdrawing AEDs where KDT is successful.
Conclusions: KDT may not be suitable for every r(20) patient, but there is a strong consensus that it should be considered as an early intervention. In the UK, NHS KDT services are predominantly available for paediatric patients, with very limited adult access. A detailed health economic analysis illustrating reduced acute care costs and improved quality of life may encourage more widespread KDT implementation.

Poster No. 139
Should rapid whole exome sequencing be the first line investigation for critically unwell children hospitalised with a suspected neurogenetic condition?

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Objectives: Whole exome sequencing (WES) with a 2-week result turnaround time has become available on the NHS for children in an Intensive Care setting. We aimed to determine the diagnostic utility and impact on clinical care of WES in a regional Paediatric Neurology Centre.
Methods: Retrospective case notes review.
Results: Six cases (4M, 2F) were identified. Three patients were dependent on long-term respiratory support. A pathogenic mutation was detected on WES in 5/6 cases (83%). One case required 'reverse phenotyping' with an abnormal transferrin glycoform electrophoresis confirming that two heterozygote variants of the RTF1 gene were consistent with a Congenital Disorder of Glycosylation (CDG). No other variants of unknown significance were found. Three children presented with neonatal onset epileptic encephalopathy (two cases had SCN2A, one case WWOX), one child with intractable epilepsy from 2 months of age (RFT1 mutation associated with CDG) and one child with hypotonia and ventilator dependence after a respiratory infection at 4 months of age (IGHMBP2 mutation associated with Spinal Muscular Atrophy with Respiratory Distress). WES found no pathogenic mutation in a 3-year-old with intracranial calcification, microcephaly, epileptic encephalopathy and severe developmental regression. In 5/6 cases other single genes/panels had been sent prior to initiation of WES with multiple single genes/panels sent in 3/6 cases. In 3/6 cases WES detected the gene thought most likely based on clinical phenotyping on the request form.
Conclusions: WES has a high diagnostic yield in this cohort of patients. Reaching a prompt diagnosis facilitated withdrawal of care in one case (IGHMBP2) and helped to exclude an epilepsy surgery hypothesis in four cases as well as guide prognosis in all cases. WES should be considered as a cost-effective alternative when multiple single genes and/or genetic panels are being sent off in parallel due to clinical urgency.

Poster No. 140
End of life care in PICU across the UK

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Objective: The care provided in the time surrounding the death of a child shapes long-term memories and has potential to impact on the grieving process. There are no specific guidelines for PICU staff in relation to what good care looks like at this time. We sought insight into practice across the UK to build an evidence base, improve care provided and share good practice.
Methods: A 10 question, anonymous, Likert survey was developed. The questions included: facilities available; Advance Care Plans; communication; patient transfer to home/hospice; follow-up for families; and training and support for staff. PICS Study Group disseminated the questionnaire to PICUs across the UK.
Results: We received responses from 21/30 PICUs contacted (RR 70%). Around 60% of PICUs have a designated cubicle for end-of-life care. Only 21% have ACPs in place for life-limited patients admitted to PICU. 79% stated relatively low uptake of hospice/home transfer for end-of-life care. 65% of units have Palliative Care Nurses coordinating care. Staff training is low, with no specific training in 30%. 55% provide a bereavement care pathway. Staff debrief only occurs in 50%.
Conclusions: From the survey feedback, we found this was an area that all units believe can be improved. In relation to ACPs, we hope this will be more widely introduced. We know that 60% of patients admitted to PICU are life limited. These difficult conversations with family help guide management, understand wishes, and formal documentation ensures all staff are aware. Several units with higher uptake of hospice/home care found early conversations with families beneficial. Units with a dedicated palliative nurse stated this allowed more time with families. We believe this should become a standard of care. Staff training is limited in most units. For something so difficult and frequently encountered, it is vital we equip staff better.

Poster No. 141
Prioritising children with epilepsy in the first seizure clinic

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Objective: Rising demand for limited First Seizure Clinic appointments was leading to increasing waiting times and the feeling that children with epilepsy were waiting too long for their first assessment. Concern was also expressed that families were not receiving our First Seizure Leaflet or given instructions about capturing any further episodes either on video or by making a written record when initially seen.
Methods: From April 2018 all families were sent a letter acknowledging the referral and asking them to contact the specialist epilepsy nurse if they had any concerns prior to the appointment. Later modifications included a seizure information leaflet and a seizure record document. We have analysed the results of the first year of using this system. Patients were identified from the clinic database and further information was obtained by reviewing clinic letters.
Results: Our initial concern that the specialist nurse would be inundated with phone calls from worried parents were not realised as only 13% (14/104) of parents contacted the service before their appointment. These were invariably parents whose children had had a second episode (10/14). 8 had had further generalised tonic clonic seizures. 11 children had EEGs performed before their first appointment. This included all the children given a diagnosis of epilepsy. 71% of these children (10/14) were given a diagnosis of epilepsy made

compared to 19.5% of other referrals ($p<0.01$). Although a higher percentage of families who were reminded about videoing any further episodes did so the difference between the two groups was not statistically significant. Unfortunately, overall waiting times were not affected.
Conclusions: A simple change to the way in which the service is delivered has led to earlier identification of those children with epilepsy. We are looking at other ways of improving the accuracy and timeliness of the appointments.

Poster No. 142
Children's headache network idiopathic intracranial hypertension guideline development group: a collaborative effort

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Introduction: Paediatric Idiopathic intracranial hypertension (IIH) is an uncommon disorder and presentation is varied with children presenting to paediatricians, paediatric neurologist, and ophthalmologists. There are many areas of diagnosis and management where evidence is limited. A national adult evidence and consensus-based guideline was published in 2018. No national paediatric guideline exists to aid the further investigations and management of the cases. The IIH meeting at the BPNA conference in 2017 and January 2019 set the scene for collaborative work on this topic.
Aim: To develop a national paediatric IIH guideline based on the available literature such as modified Dandy criteria, Friedman 2013 classification and ICDH-3 classification and consensus amongst various members of BPNA CHAN group, Members of RCPCH, Ophthalmology, neurosurgery and radiology, and patients.
Methods: A core Children's headache IIH guideline development group was established and has met at four national special interest group meetings between November 2017 and September 2019. Topics discussed include incidence of papillioedmea, CSF dynamics in IIH, BPNSU IIH data, Ophthalmology good practice, Regional IIH pathways in UK and setting up of the Delphi process. The paediatric IIH study day in September 2019 with invited patient/parent representatives highlighted the impact on families with the disorder with need for better communication about the disorder, clear guidelines and sharing of good practice amongst clinicians. An email list of BPNA CHAN group, RCPCH members, ophthalmologists interested in the guideline was created.
Results: A set of 55 statements were drafted for Delphi consensus work. These are currently being reviewed by the core guideline development group prior to being circulated to the wider working group.
Conclusions: Goal setting for the next process with the Delphi process to work with the core committee and a wider working group will be presented at the BPNA conference 2020.

Poster No. 143
The Chameleon Project: a children's end of life care quality improvement project

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Objective: NHS England's Marginal Rate Emergency Threshold (MRET) and Readmission Fund funded the Chameleon Project 2018 (Twitter account: @chameleonproje1), to improve children's end of life care. This funded a lead disability paediatrician with expertise in Paediatric Palliative Care (10h/wk), a children's palliative care nurse (3d/wk) a network administrator (2d/wk), and additional hours for paediatricians in the critical care, oncology, and neonatal units, and in each of the local district general hospitals (total 18h/wk).
Methods: Tools were developed to aid identification of children in the last year of life and to support anticipatory care planning. The team attended ward rounds and provided teaching sessions, advice and support. Children who died an expected death in the 12 months of the project were ascertained from the child death review teams. Non-elective admissions, bed days, and costs were tabulated. We also evaluated the documentation of care plans and post bereavement family feedback questionnaires.
Results: 29 children died an expected death. The same number died during the previous 12 months. The median number of non-elective admissions reduced from 2 to 1 per child, specialist ward bed days reduced from 504 to 251 (50% reduction). For children admitted to PICU in the last 12 months of life, the total PICU bed days reduced from 342 to 184 (46% reduction), the median length of stay reduced from 21 days to 11 days, and the maximum length of stay reduced from 141 days to 38 days. The percentage of children who died an expected death who had documented anticipatory care plans rose from 50% to 72%.
Conclusions: The network of clinicians with expertise in paediatric palliative care working together across a region improved anticipatory care planning and reduced admissions and bed days for children in their last year of life: better care with reduced costs.

Poster No. 144
TANGO2: an unusual cause of ataxia

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Child A, a boy with speech and language delay, presented at 2 years of age with self-resolving episodes of floppiness, ataxia, and disorientation. There was associated muscle weakness and drooling. These unusual episodes occurred 3 to 4 times per week and were often triggered by excitement, especially physical and emotional overstimulation. They lasted from a few minutes to an hour, with no residual deficit. Episodes could also be triggered by having late meals (fasting episodes). Investigations including an MRI/MRA brain, EEG, sleep-deprived EEG and video telemetry did not reveal any significant abnormalities. Metabolic and endocrine tests were normal. As his presenting symptoms were consistent with episodic ataxia, possibly a periodic paralysis spectrum, a trial of acetazolamide was given, which showed some improvement in the number and severity of the episodes. At 8 years of age, genetic sequencing results revealed Child A has a recessive 23Kb deletion within the long arm of chromosome 22, band q11.21. This is a homozygous intragenic deletion within the TANGO2 gene. TANGO2 is a 'transport and Golgi organization 2' homolog. The function of TANGO2 is unknown; however, in previous studies, depletion in Drosophila S2 tissue culture cells was observed to cause fusion of the Golgi with the ER. A recent study of 14 individuals with TANGO2, illustrated that Child A has a clinical phenotype which is consistent with those previously reported in the literature. Although seizures are present in 75% of individuals with TANGO2, Child A has not had any seizures to date. Although no effective treatments for this rare condition are known, early diagnosis is important so that individuals and their families are aware of the potential encephalomyopathic crises and arrhythmias which occur. Further research in elucidating the structure and function of the TANGO2 protein may lead to effective therapies in the future.

Poster No. 145
Magnetic resonance spectroscopy (MRS) in neonatal hypoxic ischaemic encephalopathy (HIE)

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Objective: HIE affects around 1.68/1000 live births. Prognostication relies on clinical progress, neurophysiology, neurological examination, and Magnetic Resonance Imaging (MRI). There is limited information on the relationships between MRS brain results and visual appearances of the brain on MRI and clinical features. This work studied the use of MRS in this cohort.

Methods: MRS is used routinely in all neonates with HIE in our unit, so approval for this service evaluation was obtained from our Clinical Governance Department. We identified neonates with HIE between Jan 2010 and March 2016 who had MRI and MRS in the first 7 days of life. Medical notes were reviewed, and MRI results categorised as normal or abnormal. MRS results and clinical features were compared between MRI groups using parametric or non-parametric testing. Correlation and regression analyses studied relationships between clinical features and MRS results. *P*-values of <0.05 were assumed to be significant.

Results: 82 participants were identified, 19 were excluded because they did not meet our inclusion criteria. Data from a total number of 63 neonates were analysed using R studio. Babies with abnormal MRI scans had significantly lower birth weight ($p=0.018$), gestational age ($p=0.037$), and higher scores in the Sarnat staging scale ($p=0.04$). The analysis of the MRS data also revealed that these babies had lower levels of N-acetylaspartate (NAA) in their parieto-occipital region ($p=0.006$), as well as higher levels of lactate and lactate to choline both in the parietooccipital region ($p=0.032$ and $p=0.007$ respectively). Finally, these significant MRS variables were significantly correlated with time to normalisation of lactate in single linear regression. Multiple linear regression models revealed correlations with clinical indicator like cord gases and Sarnat score.

Conclusion: This study demonstrated that abnormal MR spectroscopy markers are indicators of hypoxic ischaemic injury and are correlated with relevant clinical features.

Poster No. 146
Paediatric neurorehabilitation (PNR) units for CNS injury (traumatic and non-traumatic) – under-resourced and unequal

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Background: More children and young people are surviving with an acquired central nervous system injury (traumatic or non-traumatic). The first NHS England (NHSE) specialist specification for paediatric neurorehabilitation services was written in 2013. Evidence for benefits of early neurorehabilitaion after adult stroke are compelling – evidence for early neurorehabilitation in CYP is emerging.

Methods: Service information was collected from all England and Wales PNR units in 2019.

Results: 15/17 units contributed. Activity is increasing (464 (2012/13); 530 (2013/14); 595 (2014/15). 10/17 (60%) are major trauma units (50%) have dedicated coordinators. Several units cannot offer daily therapy. Most units discharge CYP home.

Conclusions: Considerable neurorehabilitation in-patient activity is taking place but there remains an absence of secure funding, adequate staff, dedicated beds, key members of the MDT, protected time for pro-active patient specific discharge planning. Neurorehabilitation is an integral part of the neuroscience clinical pathway and our children deserve a fully resourced service as described in the service specification.

Poster No. 147

Investigating factors that influence unplanned admissions and A&E attendances in those with pre-existing neurological conditions in childhood

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Objective: Previous papers have shown increasing demands and costs to the NHS in relation to the inpatient care of children with neurological conditions. Unplanned admissions may reflect a lack of effective care and have been shown to correlate with high outpatient clinic Did Not Attend (DNA) rates 2. The aim of this study was to determine factors underlying unplanned admissions and Accident & Emergency (A&E) attendances in a cohort of patients under the care of the Leeds regional paediatric neurology service over a 3-year period.
Methods: All children <18 years who had paediatric neurology outpatient appointments in 2013 were identified using hospital databases. Clinical and demographic data was extracted from electronic case notes. Those without a definitive neurological diagnosis or who had moved to adult services during the study period were excluded. The cohort was cross referenced to A&E databases and admission records from 2015 to 2018. Poisson regression was used to identify any correlation between specific predetermined factors to assess their influence on A&E attendance and admission rates.
Results: A cohort of 291 patients was established and 53 had a total of 82 unplanned admissions during the study period. 183 patients had A&E attendances with a total of 570 attendances. Higher DNA rates, younger age and certain diagnostic categories correlated with increased rates of unplanned admissions. The role of emergency care plans in preventing admission was unclear as only 27/147 patients with epilepsy had care plans in place.
Conclusions: This study confirms the association between increased rates of A&E attendances and unplanned admissions in children with specific neurological disorders and high DNA rates. This is relevant for service planning as it highlights the need to target scarce resources towards 'higher' risk patients with more complex diagnoses where more integrated care and support may prevent or reduce unplanned hospital attendances.

Poster No. 148

Audit comparing Great Ormond Street Hospital headache clinic diagnoses and management of patients aged 12 to 17 years to NICE clinical guidelines

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Introduction: Between 16/4/18 and 15/4/19 the GOSH headache clinic saw 85 new patients aged 12 to 17 years. The NICE Clinical Guideline 150 (CG150) on the diagnosis and management of headaches in over 12s covers tension-type headache, migraine, cluster headache and medication overuse headache. This audit aims to compare GOSH diagnosis and management to those of the CG150.
Methods: Using the patient list from the headache clinic data was gathered by accessing outgoing clinic letters via Epic. Raw data was collected on; age, gender, description of headache (pain location, quality, intensity, duration and frequency) and associated symptoms, triggers, previous imaging, previous and current treatments. The management data collected include: diagnosis and treatments offered, as well as whether GOSH offered lifestyle advice, psychology, occipital nerve block or Riboflavin. This data was then compared to CG150.
Results: 37 (62.7%) of diagnoses made by GOSH matched the CG150 diagnosis. 22 (37.3%) diagnoses differed, with 14 of these due to discrepancy between chronic/episodic and/or presence of aura and 6 due to the vague diagnoses of migraine- type, new daily persistent, migrainous etc. fitting the CG150 definition of chronic migraine. All but one patient was managed in line with the guidelines. 76.9% of patients had brain imaging prior to attending the clinic, with 21.7% of these reporting positive findings.
Discussion: Despite 22 patients' diagnosis differing between GOSH and CG150, all but one patient was managed in line with the guidelines. This is likely due to NICE recommended management being the same for any type of migraine. Improvements could be made in documentation of frequency and duration of headache and aura, as well as more routinely offered lifestyle advice, psychology and Riboflavin recorded in outgoing clinic letters.

Poster No. 149

CT head scans in children and young people in the emergency department: is it necessary and how useful?

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Objective: To review the purpose of CT head requests from emergency department of a busy tertiary hospital as part of quality improvement. Due to increasing evidence of CT scan radiation predisposing to leukaemia and brain tumours, it is best to keep CT scans to the minimum if clinically indicated. This project reviewed the indications for CT head and also looked at patients who had repeated CT or MRI head scans within 3 years.
Methods: Data was collected retrospectively looking at a snapshot period of 3 months between September- November 2018. Patients were <18 years of age and they had a CT head from emergency department at King's College Hospital, London. Trauma patients were excluded. Data was collated with aid of the neuro CT department 'CRIS' system.
Results: Out of 56 patients, reasons for CT included: head injury (29), ventriculo-peritoneal shunt blockage (13), refractory seizures/status epilepticus (5), space occupying lesion (5), orbital cellulitis (1), intracranial haemorrhage (1) and

tuberculosis/sarcoidosis (1). Out of the sub-categories, the group of refractory seizures/status epilepticus were most likely to have repeated imaging with either CT or MRI within 3 years (80%), followed by the group of ventriculo-peritoneal shunt blockage (77%), space occupying lesion (20%) then head injury (14%). Out of 5 patients with refractory seizures/status epilepticus, 4 were already known to have epilepsy. Also, most repeated imaging included a subsequent head MRI.

Conclusions: Most common indications for CT head were head injury and shunt blockage (as this was a neurosurgical centre). The groups most likely to have repeated imaging were refractory seizures/status epilepticus and shunt blockage. With children presenting with known epileptic seizures in the emergency department, it is important to consider clinical data and seek to devolve decision to image.

Poster No. 150

Isolated radial nerve palsy, a rare presentation of congenital wrist drop

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Isolated congenital radial nerve palsies are a rare phenomenon and typically spontaneously recover within 6 months. The true incidence is not known, but in a recent study 2.6% of infants presenting to a brachial plexus injury clinic had an isolated congenital radial nerve palsy. Patient A is a 10-week-old male who presented at birth with a left sided wrist drop following a non-traumatic elective caesarean section at 38+5/40. His birthweight was 4.23kg (91st centile). Movement of the wrist and digits were impaired to absent with preservation of function at the shoulder and elbow. There was a nodule noted in the left upper limb, anatomically superficial to the radial nerve. It was a normal pregnancy with no antenatal or postnatal issues. He attended physiotherapy and occupational therapy who provided a splint. On examination at 10 weeks, there was weakness of the extensors of the left wrist. The 3rd, 4th and 5th digits remained fully flexed at rest and could be extended passively but not actively. Extension of the thumb and index finger had recovered at 10-week review. Function at the shoulder and elbow joints were preserved with normal flexion of the wrist and digits. A scar was noted superficial to the radial nerve at the same location as the lesion described at birth. The remaining systemic and neurological examinations were normal with typical development and appropriate growth. The working diagnosis at present is an isolated radial nerve palsy likely caused by in-utero compression. The nodule and scar noted above are consistent with lesions described in a previous case series. These were hypothesised to be areas of fat necrosis secondary to compression; resulting in the palsy. Patient A's lack of further neurology such as a generalised brachial plexus palsy makes a birth injury less likely. Further investigations and follow-up are awaited.

Poster No. 151

An audit of the use of valproate in girls of childbearing age with moderate, severe and profound intellectual disability

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Background: Valproate is an effective antiepileptic medication. If a woman becomes pregnant while taking valproate, her baby is at risk of congenital malformations (1 in 10) and developmental disorders (4 in 10). Furthermore, it is associated with an increased risk of autism spectrum disorder and ADHD. In 2018, the NHS/HSE recommended new restrictions on the use of valproate, including a national Pregnancy Prevention Program (PREVENT) and avoidance in prescribing to female patients of childbearing potential unless other treatments are ineffective or not tolerated.

Objective: To review the use of valproate in a well-defined population of at risk females with moderate to profound intellectual disability (ID). Identify the patients at risk and imbed the guideline into our practice.

Methods: A retrospective chart review was carried out of all girls aged between 6 and 18 years, attending the Daughters of Charity Disability Service (DOC) in Dublin, Ireland. Data such as diagnosis, valproate use, degree of ID/Gross Motor Function Classification System (GMFCS), documentation of menarche and discussion regarding risk of valproate use were recorded.

Results: In total 9 females aged between 6 and 18 years where identified as currently using valproate out of 73 charts reviewed (12%). Of the 9 patients identified, 2/9 had moderate ID (GMFCS III) and 7/9 had severe to profound ID (GMFCS IV–V). 3/9 had menarche documented. 2/9 had the risk of valproate discussed.

Conclusions: In our cohort, a significant number of girls remain on valproate. 22% complied with new guidelines regarding discussions around the risks of valproate; highlighting the 78% of patients in need of counselling. An annual risk acknowledgement form was placed in their charts to prompt discussion next visit. In children with intellectual disability, conversations regarding contraception are difficult but essential. If valproate is used, then the risks must be fully understood by parents and carers.

Poster No. 152

Evaluation of the management of children up to age of 10 years with cerebral palsy in Southend University Hospital

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Objective: This study was to evaluate management and quality of care of children up to 10 years age with cerebral palsy in a

large District University General Hospital against NICE guidelines (NICE Guidelines NG62).
Methods: Clinic notes of all 42 registered children with cerebral palsy (CP) up to 10 years of age as of June 2019 were included in the study. This was because there was no early data on children above 10 years age.
Results: 22 patients were age 0 to 5 years and 20 patients age 6 to 10 years. 15 were male and 27 females. 11 had hemiplegic, 3 quadriplegic, 18 diplegic and 10 dystonic CP. Only 27 (64%) had GMFCS levels recorded. 11 (26%) were <28 weeks, 18 (42%) were 29 to 36 weeks and 13 (31%) were term. MRI head findings: white matter changes including PVLin 29 (69%), 3 (7%) HIE changes, 3 (7%) basal ganglia changes, 3 (7%) congenital brain malformation, 2 (4%) infarction. 1 migrated to area with no MRI report. All the children received multidisciplinary team (MDT) input including physiotherapy. Comorbidities were – children on medications for gastro-esophageal reflux -9 (with 6 PEGinsertions). For epilepsy -5, for dystonia/spasticity -5, for constipation -12, for poor salivary control -2. Behavioral issues noted in 7 and 1 was on ADHD medications. 8 had botulinum toxin injections and 4 had selective dorsal rhizotomy for spasticity. Documented discussion of diagnosis with family was in 28 (66%) patients and none in 14 patients (31%). Only 50% patients had Vitamin D levels checked.
Conclusions: Management was in line with NICE guidelines. They all had MDT input. There is a need to improve documentation of -Evidence of discussion with parents, GMFCS level by age 2 ½ years plus, hip surveillance from age 2 years for GMFCS level III to V and Annual vitamin D levels especially for GMFCS level III to V, PEG fed and children on multiple anti-epileptic medications.

Poster No. 153
Intracranial hypertension in children: an updated systematic review

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Objective: Our goal is to provide an overview on paediatric intracranial hypertension.
Methods: Given that the last update of the diagnostic criteria of idiopathic intracranial hypertension was published in 2002, a thorough Medline search of all English articles was conducted between 2002 and 2019.
Results: Intracranial hypertension may be primary, with a paediatric annual incidence ranging between 0.63 and 0.71 per 100 000 children or arise from a secondary cause. Misdiagnosis or delayed intervention can lead to poor quality of life and morbidity. In 2013, this condition was reconsidered, due to new accepted values for opening pressure and advances in neuroimaging; the importance to develop effective therapeutic strategies in order to prevent blindness was thus highlighted. To date, the main strategies described involved both medical and surgical approaches; nevertheless, there have been no paediatric intervention studies. Disease monitoring plays a key role in the definition of the best timing and modality of treatment. Recently, a risk stratification has been proposed with the aim to facilitate an adequate evaluation and proper care of children with intracranial hypertension: visual monitoring could represent an objective tool to manage these patients. In recent years, important evidence for the efficacy of acetazolamide emerged in the Idiopathic Intracranial Hypertension Treatment Trial. Surgical treatment is the modality of choice in children with worsening vision impairment, intractable headaches despite maximal medical management or in case of intolerance to medical therapy.
Conclusions: There are poor evidences about paediatric intracranial hypertension's outcomes. Unfortunately, children's quality of life is heavily influenced by pain and permanent vision loss. Standardized therapeutic strategies remains uncertain, highlighting the need for longitudinal studies to identify the best treatment in childhood. In order to alleviate symptoms and prevent permanent chronic sequelae, careful clinical evaluation and ophthalmological monitoring could be a useful guide to better manage this medical condition.

Poster No. 154
Cerebral venous sinus thrombosis with secondary intracranial hypertension: a case report and review of the literature

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Objective: Cerebral sinovenous thrombosis in childhood is a life-threatening neurological entity with uncertain epidemiology, potentially complicated by secondary intracranial hypertension. In the literature, there is a lack of evidence supporting the main strategies to approach both these medical conditions. Our objective is to highlight the value of a prompt diagnosis aiming to define a tailored management approach based on children monitoring.
Methods: We review the main findings regarding cerebral sinovenous thrombosis and intracranial hypertension in children through illustration of a case with otogenic sinus thrombosis and secondary intracranial hypertension.
Results: A 7-year-old boy developed a local venous sinus thrombosis because of the spreading of a primary infective process from his middle ear into the sigmoid sinus complex, facilitated by anaemia and dehydration. The venous outflow disturbances led to secondary intracranial hypertension. The management aimed to treat cerebral thrombosis with anticoagulants and intracranial hypertension through medical and surgical strategies. The insertion of the lumbar-peritoneal

shunt was necessary when medical approached failed and visual function deterioration was evident. Careful clinical evaluation and ophthalmological monitoring helped us in the tailoring of the best treatment with the aim to alleviate symptoms and prevent sequelae of increased intracranial pressure. In the literature, no paediatric intervention studies regarding the main strategies to reduce intracranial pressure have been published. Moreover, there is a lack of evidence supporting the safety of anticoagulation therapy, reducing the possibilities to safely manage cerebral thrombosis in childhood.

Conclusions: In children, a multidisciplinary approach is essential to manage both cerebral thrombosis and intracranial hypertension and ensure an optimal follow-up, aiming to prevent visual and therapy-related complications, possible relapses and their early diagnosis. From our perspective, monitoring our patient with clinical manifestations and visual status helped us to plan the best timing and modality of treatment and intervention.

Poster No. 155
KIF1A-related disorders: a wide spectrum of central and peripheral nervous system involvement

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Objectives: Mutations in KIF1A are associated with a wide range of neurological disorders, ranging from hereditary spastic paraparesis (HSP) to sensory neuropathies to a severe infantile neurodegenerative disorder. Collectively, they are extremely uncommon but likely to be under-recognised. We aim to report the spectrum of KIF1A-related disorders from a single tertiary neurology centre, with a view to improving understanding and awareness of these rare conditions.

Methods: Affected individuals known to Great Ormond Street Hospital were identified through liaison with consultants involved in the care of children and young people with movement disorders. Clinical information was collected through a retrospective review of case notes.

Results: Twelve individuals in 9 families were identified. All had heterozygous KIF1A mutations including three previously unreported variants. Severity ranged from a fatal neonatal-onset disorder with contractures, absence of visual development, and agenesis of the corpus callosum on MRI to HSP with preservation of ambulation into the second or third decade of life and entirely normal MRI. Upper motor neuron signs were found in 10/12 children and a primarily sensory neuropathy was present in 9/11 children assessed. 3/12 children also had extrapyramidal signs (dystonia). Some degree of learning difficulties and/or disorders of mood or behaviour were present in all children. Optic atrophy, MR brain white matter changes and epilepsy were also common, especially in those children who were more severely affected overall.

Conclusions: KIF1A related disorders are so diverse that it is arguably misleading to consider them as a single disease entity. Features common to the majority of affected patients include upper motor neuron involvement, and neuropathy (even in the absence of an obvious sensory deficit), with high risk of other neurological and neurobehavioural comorbidities.

Poster No. 156
Biallelic mutation of SETX and additional likely 'in cis' SETX sequence change in ataxia with oculomotor apraxia type 2

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Objective: Ataxia with oculomotor apraxia type 2 (AOA2) is a slowly progressive, autosomal recessive disease characterised by the triad of ataxia, oculomotor apraxia, and sensorimotor neuropathy that results from mutations in the gene encoding senataxin (SETX), a DNA/RNA repair protein essential for genomic stability. We investigated a 16-year old male with a history of unsteady gate for genetic and molecular changes associated with AOA2. In this report we describe a case of AOA2 with two clear pathogenic SETX mutations, one of which is novel, as well as two further SETX changes likely to be in cis polymorphisms that have previously been reported as pathogenic.

Methods: Two independent lymphoblastoid cell lines obtained from the patient were used for Western blotting of senataxin and protein markers of other autosomal recessive cerebellar ataxias. The SETX gene was sequenced to identify possible disease-causing mutations.

Results: Western blotting showed reduced levels of senataxin. Serum AFP level was elevated at 15μg/l (normal 0.0–7.0μg/l). Genetic sequencing revealed two clear pathogenic SETX mutations. One of these was a novel mutation, c.2990delG; p.(Cys997PhefsTer32), a deletion causing a reading frameshift resulting in truncation and loss of expression of senataxin protein from this allele. The other, c.6638C>T; p.(Pro2213Leu) was a missense mutation within the helicase domain which has previously only been reported in the homozygous state in a Japanese AOA2 patient. Two further sequence changes, c.1807A>G; p.(Asn603Asp) and c.1957C>A; p.(Gln653Lys), were also identified in our patient.

Conclusions: The reduced senataxin expression and elevated AFP levels support a diagnosis of AOA2 in our patient. Genetic analysis found a novel pathogenic mutation and documented the first case of another pathogenic mutation in the helicase domain outside of Japan. The case contributes to the growing diversity of SETX mutations known to be responsible for AOA2.