Poster Presentations

Poster No. 001

Diagnostic neuro-vestibular features in paediatric vestibular migraine

R CRUNKHORN[1], S RATNAYAKE[1], NF TURGUT[2], S DASGUPTA[1]

[1]Department of Audiovestibular Medicine & Audiology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [2]Department of ENT, Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Objective: Vestibular Migraine (VM) including its variant Benign Paroxysmal Vertigo of Childhood (BPVC) is the commonest cause of childhood dizziness. However, it remains underdiagnosed. Diagnosis is important as it leads to successful management. There is meagre evidence regarding neurovestibular examination/quantification in paediatric VM. The aim of this study is to investigate this important aspect to aid in the diagnostic process.
Methods: A retrospective case note review was undertaken on all patients with VM at a tertiary Paediatric Audiovestibular Medicine clinic between January and December 2018. The diagnostic criteria of VM/BPVC was based on the Barany Society criteria (2012). Children underwent intense neurovestibular examination/investigations including videonystagmography and vestibular function tests. The results were analysed and statistically evaluated.
Results: 81 children (M:F 38:43; 2–17 years) were identified. 30 (37%) had normal examination and diagnostic findings. 20 (25%) had one abnormal finding whilst 31 children (38%) had ≥2 clinical and/or diagnostic abnormalities. Abnormal central oculomotor signs were detected in 20 (25%). Neurovestibular signs to assess vestibular angular and gravitational motion sensor function were abnormal in 37 children (45%). In the whole cohort, 21 (26%) had significant semicircular canal abnormalities (low vestibular-ocular reflex (VOR) gain, high VOR gain or saccades in the video head impulse test). Vertical semi-circular canal VOR gains (anterior and posterior) were higher in the migraine group than our hospital norms (p=0.0001). Up to 90% of children who were followed up responded to migraine prophylaxis and about a third showed changes in their neurovestibular tests that were heterogeneous.
Conclusion: There is a high-yield of central and neuro-vestibular features in paediatric VM. The high VOR gain observed in the series appears to be a promising possible biomarker for VM. These findings are useful for clinical correlation at initial and follow-up assessments.

Poster No. 002

Functional neurological disorders (FNDs) in children: an observational study from a Scottish regional cohort

K YONG[1], K BURGESS[1], K HOGG[1], M LINDSAY[1], A BAXTER[1], RFM CHIN[1,2], A MCLELLAN[1], K MCWILLIAM[1], E PILLEY[1], J SHETTY[1,2], K KAMATHTALLUR[1]

[1]Department of Clinical Neurosciences, Royal Hospital for Sick Children, Edinburgh, UK; [2]Child Life and Health, MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK

Objective: FNDs are common in clinical practice. There are limited reports on epidemiology and spectrum of clinical features in children. Improved understanding of both would help clinical management and inform resource allocation towards effective therapies. We report epidemiologic and clinical data from a prospective cohort of physician-confirmed FNDs.
Methods: A database of FNDs in children under 16 has been constructed using prospective physician-confirmed cases at a tertiary children's hospital in Scotland since February 2018. Confirmed cases of FNDs were captured by weekly active email surveillance to clinicians in Emergency Medicine, General Paediatrics, Paediatric Neurology and Child & Adolescent Mental Health Service (CAMHS). Clinical presentation, investigations, treatment and outcome were collected by reviewing medical notes. All data, including missing data, were analysed in Microsoft Excel and reported; available-case analyses were performed on the distribution of associated factors and therapies.
Results: There were seventy-five children at time of analysis; median age 11 (interquartile range 9–14) years; 72% female. Forty-seven percent had more than one presenting symptom: headaches and non-epileptic seizures were the commonest symptoms (24% each in males; 30%, 28% respectively in females). Fifty-one percent had organic illnesses in addition to FNDs. Poor mental health (38%) and high sporting expectation (38%) were the commonest associated factors in males; chronic medical conditions (55%) and high academic expectation (33%) in females. Thirty-four children (45%) reported symptom improvement with the most utilised therapy being CAMHS input (64%).
Conclusions: Headaches and non-epileptic seizures are common presentations of FNDs. Co-occurring organic illnesses and FNDs is common and hence, important to recognise for appropriate management. Poor mental health, academic/sporting achievements and chronic health problems are some common risk factors. Future work including data linkage analysis for long-term health and educational outcomes are planned.

Poster No. 003

Multi-agency information sharing and medical outcomes in suspected non- accidental head injury (NAHI) at Great Ormond Street Hospital (GOSH)

P AHMED, W DOYLE, R ROBINSON

Great Ormond Street Hospital, London, UK

Objectives: A previous audit (2003–2015) identified poor communication with Health Professionals regarding the outcome of legal and care proceedings following suspected NAHI. The aim of this

DOI: 10.1111/dmcn.14749

follow-up audit was: (1) To determine the legal outcomes in children with suspected NAHI, whether clinicians were informed, and the correlation between outcome and clinical opinion. (2) To review the significance of radiological and ophthalmological findings in suspected NAHI.
Methods: A review of 37 cases of suspected NAHI assessed at GOSH between January 2015 and May 2020. Medical and social care records were used to identify the legal outcome and this was correlated with the initial clinical index of suspicion. The radiological and ophthalmological findings were correlated with the clinician assessment.
Results: The legal outcome could be determined in 23/37 cases (62%) compared to 17/41 (29%) cases in the previous audit. There was a high correlation between the clinical index of suspicion and the legal outcome. Retinal haemorrhage (RH) was identified in 62% of cases, of which 78% were assessed as high risk of NAHI. Subdural haemorrhage (SH) occurred in 78% of cases, of which 62.5% were assessed as high risk of NAHI. Of the 43% of cases with skeletal survey (SS) abnormalities, 62.5% were assessed as high risk of NAHI. Following Royal College of Radiology (RCR) guidelines, MRI whole spine and repeat SS at 11 to 14 days were performed in selected cases (33 and 16 respectively). A spine abnormality was identified in 10/33 cases. Follow-up SS in 3/16 cases enabled exclusion of a previously suspected fracture.
Conclusions: Health professionals have become better informed of the outcomes of legal and care proceedings in cases of suspected NAHI. SH, SS abnormalities and RH are considered by clinicians as strong indicators of NAHI. Additional imaging recommended by the RCR is informative in a minority of cases.

Poster No. 004

Can we predict length of rehabilitation stay based on admission patient categorisation tool score combined with rehabilitation complexity score?

S MACKIE, M GEARY, J PALMER, J PELLING, G BIRD-LIEBERMAN
Paediatric Neurology, UHS NHS Foundation Trust, Southampton, UK

Background: Our neuro-rehabilitation service provides early intensive rehabilitation to patients with a newly acquired neurological injury, often starting in PICU. We collect data as per UKROC, including patient categorisation (PCAT) and rehab complexity scores (RCS), at the start of rehabilitation. UKROC assessments measure complexity, but don't dictate duration of rehabilitation.
Objective: Can we predict length of stay at start of rehabilitation based on a combination of PCAT and RCS?
Method: Retrospective review of inpatient neurorehabilitation notes over 2 years.
Results: 91 patients with acquired brain or spinal cord injuries (38/91 admitted to PICU). At the start of rehabilitation: Category A (highly complex rehabilitation needs)=21; Category B (moderately complex rehabilitation needs)=45; Category C (standard rehabilitation needs)=25; Very high RCS (16–20)=20; high RCS (12–15) =56; moderate RCS (8–11)=15; low RCS (1–7)=0. Median length of admission for all 91 patients=4 weeks (range 1–34 weeks). Category A + very high RCS score (14/21) median length of stay (LOS)=12 weeks (4–34 weeks). Category A + high RCS score (7/21) median LOS=6 weeks (3–12 weeks). Category C + moderate RCS score (10/25) median LOS=2 weeks (range 1–8 weeks). Category C + very high/ high RCS median LOS=2 weeks (1–12 weeks).
Conclusion: PCAT and RCS in combination can be helpful in more accurately predicting length of inpatient rehabilitation at first assessment. Category A patients whose RCS is not very high, on average, will have a shorter (50% in our cohort) admission, than those with a very high RCS score. Despite Category C patients having a high or very high RCS there is no difference in average length of stay in our cohort. This can help support families with preparing for their rehabilitation journeys and discharge planning.

Poster No. 005

Paediatric Neurorehabilitation in a time of Covid-19

A MURUGAN[1], J WILLAMS[2], D LUMSDEN[3], I WRIGHT[1], P SHARPLES[1]
[1]Bristol Royal Hospital for Children, Bristol, UK; [2]Nottingham Children's Hospital, Nottingham, UK; [3]Evelina Children's Hospital, London, UK

Objective: The Covid-19 related pandemic has negatively impacted NHS service provision. We investigated its effect on specialist paediatric neuro-rehabilitation services in England and Wales.
Methods: A questionnaire was sent to UK National Neuro-rehabilitation network members by survey monkey app. Questions explored: (1) centre details; (2) Covid-19 impact; (3) mitigation strategies; (4) recovery planning.
Results: 19 centres responded, including 17 Regional Neuroscience Centres; one stand-alone neurorehabilitation unit; one community-based specialist unit. 18 reported Covid-19 had had a significant impact on service provision. Six reported the impact was wholly negative; 9 mainly negative, with some positive aspects; 3 mainly positive, with some negative aspects; one was unsure. 16 reported having fewer neurorehabilitation beds than pre-Covid-19; in 2, >80% were closed; 2, 61–80%; 3, 41–60%; 7, 21–40% and 2, <20%. Six indicated they were unable to accept internal or external referrals; 3 only in exceptional circumstances. 7 centres offer full rehabilitation to existing inpatients; 11 only restricted rehabilitation. 14 had discharged inpatients early; 8 provided outpatient therapy post-discharge, 6 could not. Two-thirds of centres transferred patients out at the start of the crisis, 9 to another neurorehabilitation unit and 3 to district hospitals. Outpatient services were closed in 5 centres; operating fully (2); on a limited basis (8); on an increased basis due to reduced inpatient work (2). No community teams were offering normal services. 9 centres were concerned about service restoration in the short term; 12 in the medium term; 10 in the long term. Only 5 reported having a neurorehabilitation recovery plan.
Conclusion: Results highlight importance of developing robust neurorehabilitation service recovery plans to prevent children with acquired disability being further disadvantaged.

Poster No. 006

Does referral to neuro-rehabilitation services for children admitted via PICU predict an increased rehabilitation need and impact on total length of stay? A review of the 2018-2020 Southampton Children's Integrated Rehabilitation team (SCIRT) cohort

ML GEARY[1], J PALMER[1], S MACKIE[2], JA PELLING[1]
[1]Children's Therapy Department, Southampton Children's Hospital, Southampton, UK; [2]Paediatric Neurology, Southampton Children's Hospital, Southampton, UK

Objective: To determine if admission to PICU for specific Patient Categorisation (PCAT) groups are indicative of increased length of total inpatient stay (LOS) and increased rehab complexity determined via Rehab complexity scores (RCS-E).
Method: Review SCIRT patients discharged between April 2018 and March 2020. Patients subdivided. Group1 referred via PICU admission, Group2 other referral pathway. PCAT, RCS-E scores and LOS, prospectively collected, anonymised within UKROC dataset/internal databases, compared for both groups.
Results: 96 patients (104–8 excluded). PCAT SCORES: Group1 (n=41) A (highly complex)=54%, B (moderately complex)=39%, C (standard rehabilitation needs)=7%. Group2 (n=54) A=7%, B=54%, C=39%. PCATA Children: Total cohort RCS-E scores denote highly complex i.e.<12. Group1 had increased numbers within "very high" group (45% ≥17). Mean RCS-E on admission Group1=16.4 (range 13–20) versus 14.23 (range 13–16) Group2. Both cohorts demonstrated mean improvement with rehabilitation as reflected with mean RCS on discharge Group1=10.4 i.e. 6 point reduction, (3 demonstrated no change) versus Group2=7 (7.23 point reduction). Noticeable difference within mean LOS Group1 at 14.8 weeks versus 4.8 for Group2. PCATB children: Both cohorts categorised high complexity on RCS-E with mean scores on admission similar 14 versus 13.1. Group1 demonstrated increase level of change via rehabilitation with a mean change of score at discharge of 5.9 (although 6% no change) versus 3.5 Group2 (10% no change, 1 deteriorated). LOS 6.7 weeks Group1. Group2 4.6 weeks. PCATC children: Group1 demonstrated mean RCS-E reduction of 7.8 (mean score 14.3 on admission). Group2 demonstrated a mean reduction of 3.8 from 11.5 on admission (1 no change, 1 deteriorated). LOS was equivalent at 3 weeks.
Conclusion: LOS for patients admitted via PICU was increased within PCAT categories A or B although not with category C children. 76% of total cohort scored ≥12 within RCS-E demonstrating the high complexity of caseload across both groups. 91% demonstrated improvement in RCS-E scores with rehabilitation.

Poster No. 007

Delays in accessing medical care in children with neurological presentations during the first wave of Covid-19

H O'CONNELL, J TE WATER NAUDE
Child Health, Children's Hospital for Wales, Cardiff, UK

Objective: The Welsh Paediatric Surveillance Unit (WPSU) prospectively surveyed delays in children accessing medical care from April to July 2020. The purpose of this initiative was to define whether there was evidence of an effect of the Covid-19 pandemic on the delivery of healthcare to children.
Methods: The established methodology of the WPSU was employed to poll all paediatricians in Wales on a weekly basis for a 16-week period to ascertain the nature and number of children where a delayed presentation was thought to have affected their management. A pragmatic definition of 'delay' was employed, and the notifying clinicians were asked to define the nature of the impact of the delay on each referral, from minor to severe.
Results: A total of 53 children were notified to the WPSU over the 16 weeks. Seven children had delays in their being assessed by paediatricians because of neurological problems: in one case the impact on the child was defined as being severe, with a further case being assessed to have a moderate impact. The remaining 5 were thought to be minor. The nature of the problems ranged from deterioration in an existing neurodegenerative process to seizures. This contrasts with 6 cases of diabetic ketoacidosis being referred over this period, and 9 with gastrointestinal problems (primarily coeliac disease) with the impact being uniformly severe for the former group (with 2 deaths) and moderate for the latter group.
Conclusions: From this prospective study, it seems that delays in the presentation of children for medical care is less severe for neurological disorders than for children with diabetes or coeliac and inflammatory bowel disease. However, the issue of delay seems to be entrenched and pervasive. A creative solution to this is necessary.

Poster No. 008

What should Trusts charge NHS England to deliver specialist inpatient neurorehabilitation in a regional paediatric neuroscience center?

L SHUYU[2], H SMITH[2], A SPRAY[1], PM SHARPLES[1]
[1]Bristol Royal Hospital for Children, Bristol, UK; [2]University of Southampton CORMSIS team, Southampton, UK

Objective: To calculate what bed-day tariff a paediatric Regional Neuroscience Centre (RNSC) should charge to deliver a specialist in-patient neurorehabilitation service.
Methods: Ethical approval was obtained. Anonymized data on children receiving in-patient neurorehabilitation at a RNSC (1/6/2017-31/5/2019) were analyzed. Patient dependency/rehabilitation complexity was assessed by Rehabilitation Complexity Scale (RCS), which measures Care or Risk, Nursing, Therapy, Medical and Equipment needs. RCS-Extended (version-13) was scored by the multi-disciplinary team at weekly clinical meetings. RCS-E scores were categorized as: very low level of rehabilitation need (0–4); low level (5–8); medium level (9–12); high level (13–16); very high level (17–22). Discrete-Event Simulation (DES) simulated in-patient work flow, calculating how many patients would be treated daily and their changing rehabilitation needs. Staffing numbers were based on modelling results, applying published staffing provisions for adult neurorehabilitation centers. Service costs and bed-day tariffs were calculated, assuming 25% overheads.
Results: The database contained 114 children who received inpatient neurorehabilitation 2017 to 2019. 21 had no RCS data; 29 were admitted before the study period, 4 discharged after. Excluding these patients, 69 were used in the model, which mapped routes between dependency levels. Modelling estimated 91

patients to be admitted and discharged by the neurorehabilitation service over 2 years (95% CI 75–107). Mean length of stay=53 days (95% CI 44–62). Mean number of beds occupied by neurorehabilitation in-patients=6.3 (95% CI 4.8–8.0). Of these, 0.65 (95% CI 0.17–1.26) were occupied by patients with very high needs; 1.73 (CI 1.08–2.45) high needs; 2.25 (CI 1.58–2-91) medium needs; 0.20 (CI 0.13–0.28) low needs; 0.08 (CI 0.02–0.17) very low needs. Applying published adult staffing standards to the modelled complexity/dependency levels and assuming 25% overheads, the bed-day tariff required to support the service ranged from £622.45 to £754.75.
Conclusions: Application of simulation modelling to real-world paediatric data suggests costs are similar to those charged by adult centers.

Poster No. 009

A virtual regional paediatric neurology study day

JAA HOLLAND, M CHITRE, S WHYTE, P HARIJAN
Paediatric Neurology, Addenbrooke's Hospital, Cambridge, UK

Objective: Utilization of virtual platforms for training has increased significantly in 2020, including local, regional and national events. We aimed to gather feedback on experiences of a virtual regional paediatric neurology study day hosted in East Anglia, to establish how we may learn from this in anticipation of ongoing future virtual media demand.
Methods: Post-hoc electronic structured questionnaire distributed to faculty and delegates, exploring perceived effectiveness of virtual teaching, technological acceptance and attendee engagement.
Results: 107 delegates attended morning sessions with 143 in the afternoon, with 70% questionnaire completion. Attendance was slightly higher than previous regional in-person registrar training days (typically 80–90 attendees). Delegates gave feedback on a 5-point Likert scale (strongly disagree [0] to strongly agree [5]). Median scores for effectiveness in achieving registrar level competencies were 4 (quartile range 4–5), and for the format overall in achieving competencies 5 (quartile range 4–5). Median ratings for perception of videoconference delivery allowing individual participation were 4 (quartile range 4–5), and for this format's suitability for non-neurology training 5 (quartile range 4–5). Qualitative feedback from faculty highlighted that whilst active audience participation was perceived to be important for delivering effective training, such interaction was found more challenging in the virtual setting.
Conclusions: Overall, our survey presents encouraging results to support using virtual media for delivering training. Despite a high response rate, validity and generalizability of these perceptions is unknown. Positive bias may have been present, since this elective virtual study day proceeded in the absence of a mandatory in-person study day. The impact on delegate well-being through lack of socializing and networking facilities is also unknown. Notwithstanding these limitations the feedback positively supports the potential to deliver future paediatric neurology teaching using a virtual platform.

Poster No. 010

Stereotactic irradiation in pediatric patients with neurofibromatosis type 2 and cranial nerve schwannomas: tumor control and functional outcome

SV ZOLOTOVA, ES MAKASHOVA, MV GALKIN, AV GOLANOV
Radiotherapy, Burdenko Neurosurgical Institute, Moscow, Russia

Neurofibromatosis 2 type is a disorder characterized by growing of different types of benign tumors and bilateral vestibular schwannomas. Despite a long history of research, reaching of tumor control remains an unsolved problem, especially for rare tumors. The last treatment guidelines were published in 2011, and surgery was indicated how prefer treatment method. Nevertheless, surgery does not allow save the level of neurological status. Another option for this patient is a stereotactic irradiation but this method has very little basis of evidence in childhood. In our retrospective series we analyze treatment result in 13 patients with neurofibromatosis 2 type and different cranial schwannomas: 11 of vestibulocochlear nerve and 2 of caudal cranial nerves. Patients ranged in age from 5 to 17 years (mean 12.5 years). Common presenting symptoms included hearing loss (43%), tinnitus (23%), facial neuropathy (15%), sensory loss (15%) and symptoms, connection with caudal cranial nerve involvement. Median of tumor volume was 0.75 (max-10, min-0.2). Fractionation regimes were dependent on tumor volume and level of hearing. Hypofractionated radiotherapy was applied in most patients and we used radiosurgery only in one case. The median follow-up time was 74.4 months (min-24mo, max-168mo). The tumor control was achieved in all patents. Radiation-induced changes ("central necrosis") in schwannoma was developed in 5 patients according to MRI data and were regressed after 2 years of observing. Tinnitus was decreased after radiotherapy in one patient, tinnitus increased in another patient, and one patient noted hearing improvement. After treatment, one case developed trigeminal radiation neuropathy without paresthesia. Radiotherapy in pediatric patients with neurofibromatosis 2 type can be effective and save method for cranial nerve schwannomas.

Poster No. 011

Lumbar puncture: consent and complications

JAA HOLLAND, A CLARKE
Paediatric Neurology, St. George's Hospital, London, UK

Objective: Lumbar puncture (LP) is a safe and useful procedure. Consent should be obtained beforehand, including appropriate risk-benefit explanation. In spite of its low risks there is often anxiety amongst patients regarding complications. We conducted a retrospective review of LPs performed in a tertiary paediatric hospital to ascertain how consent is being taken in practice and to identify the incidence of complications.
Methods: Retrospective review of 125 CSF samples taken at St. George's Hospital, London, 1st May to 1st July 2019 inclusive from patients aged less than 18 years. Neonatal unit patients, CSF samples not obtained via LP and patients not locally followed-up were excluded, identifying 54 instances of LP for case note review.
Results: LPs were performed in patients with median age 17 months (quartile range 1.4–79 months). The given indication for LP was infection in 55%, oncology diagnosis and treatment 24%,

raised intracranial pressure 9%, seizures 6% and other reasons 6%. No explanation of the procedure was documented to have been given in 26%. Consent was documented in 78% of LPs (52% verbal, 45% written, 2% both). The most common procedural risks discussed were bleeding (44%), infection (44%), pain/-headache (35%), failure (24%) and nerve injury (13%). The only complication documented to have occurred was headache, following 6% of LPs.
Conclusions: From our data it is concerning that 22% of LPs had no documented consent. The reported 6% of LPs associated with headaches is similar to previously published studies. It is likely that mild complications such as local pain are under-reported due to the median age of patients undergoing LP and possibly negative bias towards such documentation by staff. We would advocate that patients and families are offered consistent explanation of LP to enable informed consent and to help offer clear factual information of the procedure's low risks.

Poster No. 012
A rare case presentation of paediatric catatonia - forgotten but not gone!

K TORNE
Nanavati Super Speciality Hospital, Mumbai, India

Introduction: A teenager with mutism and catatonia was treated successfully with Benzodiazepines and atypical antipsychotics.
Material: A 15-year-old adolescent presented with high grade fever on and off for 1 month. Headache over both temporal sides, inappropriate laughter, reduced speech, and interaction for 2 weeks. Noted urinary incontinence, insomnia, and excessive daytime sleepiness for 4 days. On examination noted to be disoriented and disinterested in the surrounding with mutism, catalepsy, waxy flexibility, negativism, and posturing. Past history of depression in the form of loss of appetite, disturbed sleep, social withdrawal for the last few years. Differentials' like infectious and autoimmune encephalitis, endocrine abnormalities, electrolyte imbalance, drugs induced catatonia, schizophrenia, major depression were considered.
Method: EEG, MRI Brain, and spine normal. CSF routine and IG were normal. Due to financial constraints, the autoimmune encephalitis panel could not be sent.
Results: He was treated with high pulse steroids and tapered off over 6 weeks. In a view of catatonia, injectable Lorazepam and Risperidone were given. Symptoms improved dramatically with Lorazepam within 24 hours. After 3 months of Lorazepam and Risperidone, he improved significantly.
Discussion: In developing countries due to economic limitations, where the differentiation between organic and non-organic catatonia is difficult, the temporal sequence of clinical events and immediate response to benzodiazepines can be extremely helpful as non-organic catatonia responds immediately to benzodiazepines. This treatable disorder is often overlooked as it is rare in the paediatric population. A neurobiological dysregulation in the neurotransmitter pathway is considered as a cause of catatonia as current pharmacological interventions modify GABA A, dopamine, and glutamate systems
Conclusion: Catatonia is a severe psychomotor syndrome with an excellent prognosis if recognized and treated appropriately. Benzodiazepines have been the first-line treatment for almost all types of catatonias. A precise diagnosis and high index of suspicion are mandatory to avoid death and secondary complications.

Poster No. 013
Ouch! My legs hurt

OM KAZEEM[2], R ARORA[1]
[1]*Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK;*
[2]*Queen Elizabeth Hospital, King's Lynn NHS Foundation Trust, King's Lynn, UK*

Background: Lumbar spinal stenosis (LSS) seldom affects children, albeit is very common in the adult population.
Methods: Here, we report a paediatric case of LSS. Our patient is an overweight 15-year-old boy with a 1-year history of progressive neurogenic claudication in both calves. His pain was exacerbated by standing and ambulation but was relieved by resting and forward flexion of the lumbar spine. The pain was detrimental to his quality of life and he also experienced weight gain because he was unable to remain active. The patient's past medical history was unremarkable but there was a family history of Forestier disease (diffuse idiopathic skeletal hypostosis) in maternal grandmother. Further history was negative for rheumatological, or metabolic disorder. He denied any history of trauma. On physical examination, our patient presented mild pain on palpation of the lumbar spine. Straight leg raising test was negative, and he had no neurological deficits. Examination of the peripheral circulation (both arterial and venous) was normal. X rays featured no skeletal dysplasia. Biochemical, haematological, and metabolic evaluations were unremarkable. Lumbar MRI showed constitutional narrowing of lumbar spinal canal with severe L4 L5 stenosis and flaval hypertrophy, establishing the diagnosis of LSS. The patient's symptoms slightly improved on conservative management. He is currently under regular follow-up and awaiting genetic evaluation and surgery.
Discussion: LSS with neurogenic claudication is a rare paediatric presentation. The diagnosis is based on clinical presentation and evidence of lumbar stenosis on either CT or MR imaging. LSS is managed either conservatively (NSAIDS, physical therapy, epidural injections, weight management) or surgically in refractory cases.
Conclusion: Even though LSS is not a common cause of calf pain in paediatrics, it should be taken into account and should be thoroughly investigated.

Poster No. 014
Successful neuro-rehabilitation in a 13 year old with locked-in syndrome

A MURUGAN, T SMALLBONE, L HUTCHINS, R MUIR, H CULLIMORE, G SMITH, P SHARPLES
Bristol Royal Hospital for Children, Bristol, UK

Objective: Locked in syndrome (LiS) is a rare condition and there is little information about prognosis, especially in children. We present a paediatric case of LiS.
Clinical details: A 13 year old girl, previously fit and well, presented with severe headache. Her conscious level rapidly deteriorated. Neuroimaging demonstrated posterior fossa hemorrhage with hydrocephalus. Investigation revealed a right inferior cerebellar artery dissection and ruptured pseudo-aneurysm. A COL5 mutation of uncertain significance was identified. She had a

stormy ICU course, with raised ICP requiring a posterior fossa decompressive craniectomy and Ventriculo-Peritoneal shunt. She sustained bilateral brainstem infarction, with marked autonomic instability. She required tracheostomy and nasogastric tube (NGT) feeding. As her medical condition stabilised, she remained immobile, failing to obey commands, localise pain or vocalise/verbalise. However, she could blink and move her eyes. Multidisciplinary assessment, demonstrated she could reliably communicate by eye blinking/movement, confirming a diagnosis of LiS. Discussions with parents concluded she should be actively managed, despite prognostic uncertainty. Multidisciplinary neurorehabilitation therapy was commenced accordingly. Initially, she had profound four limb weakness, incontinent, fed by NGT, had a tracheostomy and was fully dependent for al cares and used communication aids. At discharge, 20 months post-admission, she had full range of arm movements and good fine motor control. Her legs were weaker, but she was able to transfer from chair to toilet/bed/car, and walk short distances with assistance. She could talk, though dysarthric. She had significant dysphagia, was NGT fed but taking small amounts orally. Neuropsychological assessment demonstrated age-appropriate cognitive functioning. She returned to mainstream school to study GCSEs, with reduced curriculum to manage fatigue. When last seen in outpatients, she was making progress with community input.
Conclusion: LiS is a rare condition, requires input from an experienced multidisciplinary team to diagnose. Outcome in children can be good with early intensive neurorehabilitation.

Poster No. 015

An uncommon cerebral mass lesion – zebra amongst horses

M AGABNA[1], A ISRANI[1], K OYEDOKUN[1], D DU PLESSIS[2,3]
[1]Paediatric Neurology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [2]Department of Paediatric Histopathology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [3]Cellular Pathology, Greater Manchester Neuroscience Centre, Salford Royal Hospital NHS Trust, Salford, UK

Case report: A 3 year old boy, with no adverse perinatal events and developmentally appropriate for age presented with acute onset of prolonged right sided focal seizures with secondary generalisation. There was no preceding history of fever, trauma, infection or recent vaccination, and no family history of epilepsy. General physical and neurological examination were unremarkable. CT Head revealed a large area of hypodensity involving the left cerebral hemisphere with a focus of hyperdensity, representing calcification or haemorrhage in left paramedian region. MRI Brain showed a single area of extensive but well localised signal change radiating out from the corpus callosum and affecting the left posterior parietal white matter without diffusion restriction or abnormal enhancement. MR Spectroscopy, MRA and MRV were normal. There were no foci of haemorrhage on SWI sequence. MRI spine was normal, which was undertaken to see for any metastatic seeding or demyelination in the spinal cord. Other investigations including workup for autoimmune and metabolic disorders as well as CSF examination did not reveal any abnormality. The investigation findings were supportive of a neoplastic process more than an inflammatory process. However, a small possibility of inflammatory aetiology remained including infectious, demyelinating or vasculitic lesions. A decision to perform brain biopsy from the lesion to establish the precise nature of lesion was undertaken. Brain biopsy showed prominent perivascular spindles. Immunophenotype was consistent with diagnosis of meningioangiomatosis. The child continues to remain seizure free whilst on 2 anticonvulsant medications with no other neurological symptoms.
Discussion: Meningioangiomatosis (MA) is a rare benign cerebral cortical mass lesion of likely hamartomatous origin histologically characterised by meningovascular proliferation. It can be an incidental finding in asymptomatic patients, especially when associated with neurofibromatosis. It is important to be aware of this condition as MA can clinically and radiologically mimic a tumour, tumefactive demyelination, inflammatory mass lesion or vasculitis.

Poster No. 016

ENMC workshop #243, Reproductive options for families with maternally inherited mtDNA disease

J POULTON[1], J STEFFANN[2], JP BURGSTALLER[3], R MCFARLAND[4]
[1]Nuffield Department of Women's and Reproductive Health, University of Oxford, UK; [2]Service de Génétique Moléculaire et Institut Imagine, Universitéde Paris, Hôpital Necker Enfants Malades, Paris, France; [3]Institute of Animal Breeding and Genetics, University of Veterinary Medicine Vienna, Vienna, Austria; [4]Wellcome Centre for Mitochondrial Research, Newcastle University, Newcastle, UK

Background: An international multi-disciplinary group developed consensus guidelines for new reproductive options for mitochondrial DNA (mtDNA) related mitochondrial disease. Enthusiastic patients need appropriate counselling regarding the risks and benefits of novel techniques such as Mitochondrial replacement therapy (MRT), where clinical experience is limited. The UK Human Fertility Embryology Authority have established a rigorous regulatory framework.
Introduction: In heteroplasmic mtDNA disease, normal and mutant mtDNA co-exist and there is frequently a "threshold" level of heteroplasmy required for symptoms to manifest. Genetic counselling for heteroplasmic mtDNA disease is complicated by the "mtDNA bottleneck", whereby unpredictable fluctuations in proportions of mutant and normal mtDNA may arise between generations. The bottleneck size may vary between individuals, between mutations, and may change with maternal age. Key contributions to the bottleneck occur by the time that oocytes are mature. Heteroplasmy may change thereafter, due to maternal aging and reduced survival of "unfit" embryos. There is clear selection, but this does not eliminate the common mutations.
Genetic options: Prenatal diagnosis or oocyte donation may be appropriate for some families. Pre-implantation genetic diagnosis (PGD) is established for maternally inherited heteroplasmic mtDNA disease. MRT is now licensed in the UK. In MRT the nucleus is removed from either a zygote (pronuclear transfer, PNT) or an oocyte (maternal spindle transfer, MST) and placed into a corresponding enucleated cell at the same stage, but from a donor with normal mitochondria. MRT is an option for patients with: homoplasmic mtDNA disease (100% mutant mtDNA), eg. m.4300A>G, m.9185T>C m.11778G>A; or heteroplasmic disease with high recurrence risk.
Potential problems: Advanced maternal age and/or ill-health may prevent some patients from undergoing PGD/MRT. Diabetes, neurologic, cardiac and renal evaluation are indicated. Inferred from stem cell data, segregation of pathogenic mutant mtDNA to

high levels might occur after either MST or PNT in 15 to 20% of transfers.

Poster No. 017
Instructions and Prescripts. Paediatric Neurology and Neurodisabilty described by Thomas Willis (1621–1675)

AN WILLIAMS
Virtual Academic Unit, Northampton General Hospital, Northampton, UK

A country racked by an epidemic, marked social and economic crisis, revolutionary new tools and scientific thinking that transform the practice of clinical science. This is not the early 21st century, but the British Isles including Oxford during the 1640's to 1660's. Deciding, as an allegory of his firm Royalist sympathies, to embark upon a major series of studies on 'the offices of the braine' Willis laid the foundation of clinical neuroscience. He invented the word neurology, defined and named brain structures, overturned previous understanding of the workings of the brain and described the cerebrovascular circulation. Willis should not solely be seen as an 'adult' neurologist. Cerebrae Anatome (1664) showed a child's brain 'foolish from birth' with congenital cerebral atrophy. Pathologiae Cerebri (1667) could be seen as the true foundation of paediatric neurology with the first chapter on epilepsy in childhood, which includes case histories, post mortems and their interpretation: in one familial case series knowledge leading to effective treatment. De Anima Brutorum (1672) had a chapter 'Instructions and Prescripts of Folly and Stupidity' which would be considered today as learning difficulty. Within these works are other paediatric neurology/ neurodisability cases such as autism, childhood stroke, developmental regression, headache, cerebral tumour, cerebral venous thrombosis and pseudo- seizures. Willis was inspired by the Baconian ideas of a new philosophy. He worked as a member of the Oxford virtuosi, initially as part of the Invisible College, which after the 1660 Restoration became the Royal Society. His acknowledged collaborators include Christopher Wren and Richard Lower. His lecture notes recorded by the then Oxford Don, medical student (later successful revolutionary and philosopher) John Locke of the newborn brain being a tabula rasa, were taken up by Locke in his 'An Essay Concerning of Human Understanding' (1689) – central to the later enlightenment and still highly influential.

Poster No. 018
Medical management of arterial dissection in paediatric arterial ischaemic stroke: practices of British paediatric neurologists

N MCCREA
Paediatric Neurology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Background: Arterial dissection as a cause of paediatric arterial ischaemic stroke (PAIS) confers a significant risk of recurrence, compared with idiopathic PAIS (19% vs 4.5% in a recent prospective international study, the VIPS study). Medical management consists of anticoagulation (AC) and/or antiplatelet medication (AP). A landmark randomised controlled trial in adult patients did not reveal significant differences in outcome comparing AC with AP, and UK guidelines for adult patients state that either can be used, and for at least 3 months. Recent RCPCH guidelines for paediatric patients do not give a specific treatment pathway.
Methods: Members of the British Paediatric Neurology Association (BPNA) cerebrovascular special interest group and the wider BPNA were invited to complete a survey on their usual medical management of cranial and cervical artery dissection in PAIS. Surgical and endovascular management were not included. Responses were collected in June 2020.
Results: Nineteen colleagues responded. The majority use AC in extracranial dissection (15/19) and intracranial dissection (10/19). When AC is used, low molecular weight heparin alone is preferred (9/19), but various combinations of unfractionated and low molecular weight heparin and warfarin are also used. There was no consensus on duration, whether repeat imaging is used prior to stopping, and imaging criteria for stopping AC. 6/19 use AP following on from AC. Duration of AP varied from less than 3 months to long-term (mean 49 months). Several commented that they discuss patients within a neurovascular multi-disciplinary team, and others that standardised guidelines would be welcome.
Conclusion: There is a lack of consensus amongst paediatric neurologists in the medical management of arterial dissection in PAIS, including choice and duration of anticoagulation or antiplatelet agent therapy. National guidelines are recommended to aid clinicians to minimise the risk of PAIS recurrence with the most tolerable treatment in the paediatric age group.

Poster No. 019
Experience of childhood stroke management in a tertiary paediatric neurology unit

HS SHEIKH, M AWADALLA, M YOONG, A SILWAL
Paediatric Neurology Department, Royal London Hospital, UK

Objective: To review management of children with suspicion of stroke with respect to the Royal College of Paediatrics and Child Health (RCPCH) guideline on Stroke in children (2017).
Methods: Children presenting with suspicion of stroke from January 2018 to June 2020 to tertiary neurology unit were identified. Medical records of these children were reviewed and data was collected on a proforma.
Results: 11 children were identified (age range 1 year to 16 years; median 10 years). 6 children presented with acute hemiparesis, 2 with seizures and 1 with both; 1 presented with transient loss of consciousness and 1 was encephalopathic. 6 children presented within 4 hours of onset of symptoms, 2 between 4-12 hours and 3 presented more than 24 hours after symptom onset. Only 1 child had a documented Paediatric National Institute of Health Stroke Scale (PedNIHSS) to assess stroke severity. 5 children had brain imaging within 1 hour of arrival. Arterial ischaemic stroke (AIS) was identified in 5 children, cerebral venous sinus thrombosis in 2, Moya Moya and haemorrhagic stroke in 1 each and 2 had stroke mimics. Out of 5 children with AIS (ages 1.7, 1.7, 11, 14, 16 years) 2 had known sickle cell disease, 1 neurofibromatosis and 1 was later diagnosed with restrictive cardiomyopathy. 3 of these children presented within 4 hours of symptom onset and only 1 could be considered suitable for thrombolysis. None of these children met the 4.5 hour criteria for consideration of thrombolysis. 2 children with AIS were started on aspirin and 3 were transferred over to quaternary unit including 1 for suitability of thrombectomy.

Conclusion: PedNIHSS is not routinely used to assess severity of stroke. Majority were not able to get brain imaging within 1 hour of presentation. AIS was the most common cause of stroke; all but 1 had an underlying condition. Only 1 child could have been suitable for thrombolysis but there was a delay in establishing a stroke diagnosis. This highlights multidisciplinary collaboration between teams to expedite diagnosis and optimise management of these children, which can be facilitated by establishing a local stroke pathway.

Poster No. 020

The cerebrovascular pathology of the child is a reality: Ischemic strokes and cerebral venous thrombosis in children, about 45 cases

C BOUBIDI, A MEKKI, F BOUDOUAYA, K HADDAD, Z ZEROUAL
"A" CHU Hussein dey Algiers, Hussein dey, Algeria

Objective: Description of the clinical, neuroradiological and etiological profile of ischemic strokes hospitalized in our department.
Materials and Methods: We report 45 cases of pediatric ischemic stroke (newborns excluded) admitted to our department over a period of 5 years.
Results: The sex ratio was 1; the mean age 2.1 years; the mode of onset was a hemicorporeal motor deficit suffered in 95% of cases with brief disturbances of consciousness in 40% of cases. All received a brain MRI which allowed a topographic diagnosis; the middle territory (MCA) is the most affected 85% of cases; the aetiologies encountered are multiple (post chickenpox, SAPL moya moya, sickle cell disease, nephrotic syndrome, protein S deficiency, heart disease, etc); no aetiologies have been found in 40% of cases, the treatment depends on the etiology. The sequelae are mainly motor (80%) with lesional epilepsy in 40% of cases; we deplore 2 deaths (5%).
Conclusion: Pediatric ischemic strokes are particular due to the diversity of their etiologies and their occurrence in a developing brain; currently the therapeutic attitude is better codified, especially the use of anticoagulants.

Poster No. 021

Intraventricular haemorrhage in term neonates without significant hypoxic-ischaemic encephalopathy: a case series of eight patients

GL FISHER, SE LLOYD, A SAXENA, C THIRSK, C PATEL, P LEACH, S KVEDARAS, FM GIBBON, JA TE WATER NAUDÉ
Noah's Ark Children's Hospital, University Hospital Wales, Cardiff, UK

Objective: Intraventricular haemorrhage (IVH) most commonly occurs in preterm neonates and relates to germinal matrix fragility and haemodynamic factors. There is limited data about babies who had an IVH without moderate-severe hypoxic ischaemic encephalopathy (HIE).
Methods: We describe eight cases born >36 weeks gestation without HIE who had an intraventricular haemorrhage over a 13 year period between 2007 and 2020, attending Noah's Ark Children's Hospital for Wales, Cardiff. The data was obtained by retrospective review of medical records.
Results: A cause has only been identified in one of the eight cases. That child was antenatally diagnosed with haemophilia A. Two of the cases are siblings, but no genetic cause was found. Age at presentation ranged from day 3 to day 26. Presenting symptoms included irritability, poor feeding, vomiting, jaundice and seizures. All but two IVH's were bilateral. Six of the eight children required a ventriculoperitoneal (VP) shunt, all within five months of their IVH. Outcomes range from severe neurodisability to the achievement of normal developmental milestones and attendance at mainstream school.
Conclusion: No cause of IVH has been identified in seven of our eight cases. Two cases are still being investigated. The aetiology of IVH in preterm neonates is not fully understood, while the causes of IVH in term babies (without HIE) are even less clear. The outcomes in such cases are less clearly defined. From our small series, the severity of initial presentation or need for a VP shunt does not seem to correlate with the neurodevelopmental outcome. We hope to provide data to aid investigation and discussions with families about outcomes and suggest a protocol for investigation.

Poster No. 022

Spinal cord arterio-venous malformation – a rare and potentially reversible cause of rapidly progressive lower limb paralysis

RL SEARLE[1], A ISRANI[1], R KUMAR[1], M PUTHURAN[2], A CHANDRAN[2]
[1]Department of Paediatric Neurology, Alder Hey Children's Hospital, Liverpool, UK; [2]Department of Neuroradiology, The Walton Centre, Liverpool, UK

We present the case of a 10-year-old girl with a thoracic spinal arterio-venous malformation (AVM) – a rare condition requiring early identification and treatment to avoid progressive permanent loss of function. The girl presented to her local hospital with an overnight history of lower bodily pain. Upon waking she reported her legs felt like "jelly". She required assistance mobilising. She had no illness or family history of note. Over the next six hours she developed bilateral lower limb paraesthesia, numbness and tremulousness of the left foot. An MRI brain and lumbar spine at presentation were normal. The neurological symptoms were treated as psychological. Her lower limb weakness worsened over the next 12 hours. Over the following days she developed worsening lower truncal tone and double incontinence. By 8 days after onset of symptoms, she had a complete spinal cord syndrome with spastic lower limb paraplegia and spontaneous flexor spasm, hyperreflexia and clonus. She had no voluntary motor power in the lower limbs, impaired sensation in all modalities below the pelvis and an episode of autonomic dysreflexia. Subsequent whole spine MRI demonstrated an intramedullary ovoid lesion at T6, multiple serpiginous vessels within the adjacent spinal canal and abnormal T2 signal within the spinal cord extending to T1 proximally and T11 distally, suggesting venous congestion phenomenon. A spinal angiogram confirmed a thoracic spinal AVM with at least three sulco-commissural feeders. She underwent targeted endovascular embolization of the distal hypertrophied sulco-commissural artery. At 2 months post-presentation, our patient has an incomplete spinal cord syndrome receiving inpatient rehabilitation. Her spasticity is controlled with medications, she has improving motor strength proximally and distally but remains non-ambulatory, her

sensation is now present in her perineum but she continues to have urinary and bowel clearance problems.

Poster No. 023

Auditory symptoms in childhood syncope

J CANLAS, N HAIDER, D CHANDRAN, MAS AHMED
Department Of Paediatrics, Queen's University Hospital, Essex, UK

Background: Prodromal symptoms (pre-syncope) relating to a variety of organs such as eyes, skin, sweat gland, muscle, are well described but, up to our knowledge, literature on auditory symptoms (ASs) of childhood is sparse.
Aim: Main objectives are to examine frequency of ASs in childhood syncope and to qualitatively analyse their characteristics on the basis of onset, location, duration and type.
Method: A qualitative descriptive analysis of data on ASs collected over a prospective period involving 340 children and adolescents with syncope who were referred to us between April 2015 and April 2019.
Results: 41/340 (12%) eligible healthy patients (23 females, average age=13.6 years) with syncope reported ASs during prodromal phase of syncope. ASs included muffled hearing (21/41; 51%); tinnitus (8/41; 19.5%); hearing loss (5/41; 12%); echoing of sounds (4/41; 10%); muffled hearing/hearing loss (1/41; 2.5%); muffled hearing/tinnitus (1/41; 2.5%). ASs developed acutely (38/41; 92.5%); perceived bilaterally (41/41; 100%); and lasted up to a minute (12/41; 29%), 1 to <3 minutes (27/41; 66%), >3 to <5 minutes (2/41, 5%). None of our patients reported complex ASs in between attacks of syncope.
Comments: Characteristics of syncope related ASs include: (1) muffled hearing and tinnitus are the most common disturbances; (2) transient disturbances with full recovery of hearing to normal; (3) never occurred in isolation but accompanied by non-auditory pre-syncope symptoms; and (4) not involved hearing human voices or animal sound. The significance of ASs in syncope is one that has not been fully researched. Multisite study is needed to further examine the pathophysiology of ASs of syncope.

Poster No. 024

Can paediatric stroke be effectively managed in a district general hospital (DGH)? A case of Mycoplasma pneumoniae associated stroke treated with emergency thrombectomy.

JWG WILSON-GOLDSMITH[1], YJ JOSHI[2], GR REWITZKY[1], DK KRISHNAKUMAR[2], PH HARIJAN[2], MW WONG[1]
[1]Queen Elizabeth Hospital, Kings Lynn, UK; [2]Addenbrooke's Hospital, Cambridge, UK

Background: There has been national and international discussion about the role of specialist centres and district hospitals in managing paediatric stroke.
Case presentation: A 10-year-old previously well girl presented to a DGH Emergency Department with sudden onset reduced responsiveness, right-sided hemiplegia and expressive aphasia. CT Head showed slight high signal within the proximal left middle cerebral artery (MCA). A general anaesthetic MRI and MRA was performed which was suggestive of an extensive thrombosis, with diffusion restriction in the left MCA territory. The patient was discussed with paediatric neurology and regional PICU immediately and transported within four hours of presentation by the local anaesthetic team. Her CT angiogram showed diminished filling of the left internal carotid artery (ICA), with CT perfusion study showing a small completed infarct in the left lentiform nucleus, and a large penumbra throughout the MCA territory. At seven hours post presentation, digital subtraction angiography confirmed distal occlusion of the left ICA and she underwent a thrombectomy; followed by Aspirin. Post procedural CT head showed small left insular and perisylvian established infarct only. At discharge she was walking unaided. Stroke workup revealed a high Mycoplasma Pneumoniae titre which was treated with a course of oral macrolide. At 5 months follow up she has shown good physical improvement with some neuropsychological difficulties.
Discussion: Hyperacute arterial recannalisation therapy for Childhood Arterial Ischaemic Stroke is potentially achievable even if presentation is to a DGH. Numerous factors contribute, including frontline awareness and seamless and timely cooperation between paediatric, adult, local and tertiary teams. We would like to discuss the logistical issues involved particularly in a UK DGH setting, further challenges and offer possible solutions.

Poster No. 025

Case mix, outcome and governance in the neurovascular MDT

D GULHANE, S BHATE
Neurosciences, Great Ormond Street Hospital, London, UK

Aim: (1) To review documentation of the weekly paediatric neurovascular MDT to ensure that decisions were properly documented and recommended actions were carried out. (2) To review the data on the source of referrals and diagnosis to understand the demand and the implications of resources.
Audit standard: (1) List of the attendees, decisions and recommendations should be clearly documented. (2) The actions recommended should have been carried out.
Methods: Recorded minutes of the neurovascular MDT meetings between 1st April 2018 to 31st March 2020 were retrieved from the hospital database. A proforma was prepared listing the source and region of referral, attendees, diagnoses and decisions. Electronic Patient records were reviewed to check that there was evidence to demonstrate that advised actions were carried out.
Introduction: Great Ormond Street Hospital (GOSH), London neurovascular department provides a unique service for the whole range of neurovascular condition presenting in children. The GOSH neurovascular team comprises of neurologist, neurosurgeon, interventional radiologist, diagnostic neuroradiologist, neurovascular fellow and clinical nurse practitioner. There is a weekly neurovascular MDT. GOS is commissioned by NHS England. Whole range of neurovascular discussions are carried out in these meetings as per the referrals. Appropriate treatment is advised, and actions are taken accordingly. Advise is conveyed to the local hospitals and parents through proper channel on case to case basis.
Results: Total discussions were 691. Maximum (213) discussions were of VGAM cases followed by cPAVM (130), Stroke (89), Aneurysm (71) and Moyamoya (56). Average time between discussion and referral was 8% cases (48hrs), 24% (48hrs to 1 week), 26% (1–4 weeks) and 20% (>4 weeks). Endovascular procedure was advised in 19% of cases, radiosurgery (5%), further investigations (51%), outpatient appointments (27%).

Conclusion: MDT meetings gives model for joint work between different subspecialties and identify the requirement for funding for non-VGAM patients.

Poster No. 026
Vein of Galen malformation and congenital diaphragmatic hernia – novel association, double trouble

A ALWIS[1], R SUJATHA[2], C TOOLIS[1], S BHATE[1]
[1]*Neurosciences, Great Ormond Street Hospital, London, UK;* [2]*Paediatric Intensive Care, Great Ormond Street Hospital, London, UK*

Objective: Vein of Galen malformation (VGAM) is a rare, intracranial arteriovenous shunt causing neonatal cardiac failure and pulmonary hypertension (PH). Congenital diaphragmatic hernia (CDH) is a diaphragmatic defect through which abdominal viscera pass causing pulmonary hypoplasia and PH. Concurrence in a preterm infant with complex management and prognostic challenges are described.
Methods: Review of case notes.
Results: A 33+6 week gestation male with antenatally diagnosed CDH developed hypoxia, profound acidosis, increasing ventilatory requirements and hypotension. Echocardiography demonstrated right-heart overload and suprasystemic PH. Cranial ultrasound and MRI identified VGAM with features of prematurity and white matter ischaemia. EEG was discontinuous. VGAM, CDH and prematurity have independent associations with increased mortality and neurodevelopmental morbidity. Both malformations caused PH, which CDH repair alone would not resolve. Without hazardous VGAM intervention, worsening cardiac failure was expected. Parents were counselled for an uncertain outcome. A specialist multidisciplinary team (MDT) from intensive care, neurology, interventional neuroradiology, cardiology and surgery agreed treatment. A large VGAM was embolised on day 6 and 68 with shunt reduction. CDH was repaired on day 21. Narrow neuroprotective pH and pCO2 targets for VGAM versus permissive hypercapnia to minimise lung injury in CDH were contrary. Required ventilation for neuroprotection contributed to hypoplastic lung haemorrhage. Once neurologically stable, a degree of hypercapnia was allowed. Repeat brain MRI showed new bithalamic and splenial ischaemia. Discharge was at 1 month corrected age, in air, on diuretics and feeding orally. Sildenafil for PH was titrated to avoid theoretical increased VGAM flow. Developmental surveillance and further endovascular treatment were planned.
Conclusions: Novel association of VGAM and CDH is reported. Prematurity, high-risk treatment and dual pathophysiology compounding PH and demanding opposing ventilation strategies added complexities successfully managed by an expert MDT. Prognostication where rare conditions, e.g. VGAM, occur with significant comorbidities, is difficult. Anticipated neurodevelopmental sequelae warrants vigilant monitoring and early intervention.

Poster No. 027
CCM 1 variants in multiple cavernomas

K KALRA, AV ISRANI
Alder Hey Children's Hospital, Liverpool, UK

A 3 year old girl presented with acute onset of left sided focal motor status epilepticus of new onset involving left side of face, left upper limb and left lower limb. There was no preceding history of fever or head trauma. There was no history to suggest toxin exposure or drug overdosage. Her acute left sided focal status epilepticus was symptomatically managed by IV Lorazepam followed by IV Phenytoin loading dose and IV Levetiracetam loading dose, and then maintenance doses. There were no adverse perinatal events and she was born to non-consanguineous parents. Examination revealed absence of craniofacial dysmorphism or neurocutaneous markers. There were no apparent cranial nerve deficits. There was left hemiparesis. There were no abnormal meningeal signs or signs of raised intracranial pressure. Her MRI of the brain revealed haemorrhage in the right frontal lobe. She had an underlying cavernoma in the right frontal lobe and small cavernomas in the left parietal lobe. Due to persistence of seizures despite medication due to re-occurrence of haemorrhage in the lesion, the child underwent resection of the lesion, and has remained seizure free since then. The estimated risk of haemorrhage in cavernoma is approximately 1%/year. This risk can be cumulatively high in children and hence there is a rationale for considering respective surgery in children for cavernomas as opposed to a 'wait and watch' approach in adults. There was family history of intracranial haemorrhage in child's paternal grandmother due to cavernoma which was surgically resected. Familial occurrence of cavernomas, especially if multiple, has a strong genetic basis. Genetic testing in the child revealed pathogenic mutations in CCM1 (KRIT1 gene), the commonest gene involved in multiple cavernomas.

Poster No. 028
Onasemnogene abeparvovec gene therapy for spinal muscular atrophy type 1 (SMA1): Phase III study update (STR1VE-EU)

E MERCURI[1], G BARANELLO[2,3], R MASSON[2], O BOESPFLUG-TANGUY[4], C BRUNO[5], S CORTI[6], A DARON[7], N DECONINCK[8,9], L SERVAIS[10], V STRAUB[11], H OUYANG[12], S TAUSCHER-WISNIEWSKI[12], D CHAND[12,13], N MENDONCA[12], A LAVROV[12], F MUNTONI[3,14]
[1]*Department of Paediatric Neurology and Nemo Clinical Centre, Catholic University, Rome, Italy;* [2]*Developmental Neurology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy;* [3]*The Dubowitz Neuromuscular Centre, University College London, Great Ormond Street Institute of Child Health London, UK;* [4]*I-Motion Institut de Myologie, Paris, France;* [5]*Translational and Experimental Myology Centre, Istituto Giannina Gaslini, Genoa, Italy;* [6]*IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Milan, Italy;* [7]*Department of Pediatrics, Centre Hospitalier Universitaire de Liège, Liège, Belgium;* [8]*Ghent University Hospital - UZ Gent, Gent, Belgium;* [9]*Hôpital Universitaire des Enfants Reine Fabiola (HUDERF), Université Libre de Bruxelles (ULB), Brussels, Belgium;* [10]*MDUK Oxford Neuromuscular Centre, University of Oxford, Oxford, UK;* [11]*Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK;* [12]*Novartis Gene Therapies, Bannockburn, IL, USA;* [13]*Department of Pediatrics, Washington University School of Medicine and St. Louis Children's Hospital, St. Louis, Missouri, USA;* [14]*NIHR Great Ormond Street Hospital Biomedical Research Centre, UCL Great Ormond Street Instt. of Child Health, London, UK*

Objectives: Onasemnogene abeparvovec, a one-time intravenous gene therapy, is designed to address the genetic root cause of SMA1. Here, we report preliminary efficacy and safety results from the ongoing multicentre, open-label, single-arm, single-dose, Phase III STR1VE-EU study.
Methods: Efficacy outcomes were independent sitting ≥10 seconds (sec) throughout 18 months, survival (no death/permanent

ventilation) at 14 months. Safety outcomes were reported AEs, vital signs, cardiac and laboratory evaluations, physical examinations, and concomitant medications.
Results: Enrolment is complete (data cutoff: 31 Dec 2019; n=33, all 2xSMN2). Mean age at dosing: 4.1 months; mean duration in study: 10.6 months; mean age at last visit: 14.6 months. At baseline, 10/33 patients (30.3%) required nutritional support and 9/33 (27.3%) required ventilatory support. As of the data cutoff, six patients (18.8%) achieved independent sitting ≥10 sec (WHO criteria). Overall, 32/33 patients (97.0%) have survived without permanent ventilation. Confirmed motor milestones include eight (25.0%) rolled from back to sides, eight (25.0%) sat independently ≥30 sec (Bayley #26 criteria), and one (3%) walked with assistance. Mean baseline CHOP INTEND score (27.6) increased 5.9 (n=31), 10.1 (n=29), and 13.3 (n=27) points at 1, 3, and 6 months post-treatment, respectively. One death was reported, assessed as treatment-unrelated. Most frequently reported serious and related events included elevations in liver transaminases and pyrexia. All transaminase elevations were without associated clinical symptoms and all resolved (with the use of prednisolone in some cases). No temporal relationship could be established with prednisolone dosing. Transient platelet decreases (<75,000) were observed in four patients without associated clinical sequelae. Cardiac adverse events were not clinically significant. Elevations of troponin I concentrations were noted; all resolved without intervention.
Conclusions: The STR1VE-EU interim results continue to demonstrate the therapeutic benefits of onasemnogene abeparvovec for patients with SMA type 1. The overall benefit-risk profile of onasemnogene abeparvovec remains favourable.

Poster No. 029
Longer-term effects of Nusinersen on motor function outcomes based on age at treatment initiation

L SERVAIS[1], RS FINKEL[2], J KIRSCHNER[3], E MERCURI[4], DC DE VIVO[5], E BERTINI[6], R FOSTER[7], G GAMBINO[7], D RAMIREZ-SCHREMPP[8], R CHIN[8], S GARAFALO[8], W FARWELL[8]
[1]Department of Paediatrics, MDUK Oxford Neuromuscular Centre, Oxford, UK; [2]Division of Neurology, St. Jude Children's Research Hospital, Memphis, TN, USA; [3]University Hospital Bonn, Bonn, Germany; [4]Università Cattolica del Sacro Cuore, Roma, Italy; [5]Columbia University Irving Medical Center, New York, NY, USA; [6]Post-Graduate Bambino Gesù Children's Research Hospital, Rome, Italy; [7]Biogen, Maidenhead, UK; [8]Biogen, Cambridge, MA, USA

Objective: Evaluate the longer-term effects of nusinersen on motor ability by age at treatment initiation.
Methods: ENDEAR was a randomized, double-blind, sham procedure-controlled study of nusinersen in infants with 2 SMN2 copies and symptomatic infantile-onset SMA. ENDEAR participants could enroll in the open-label SHINE extension study. NURTURE is an ongoing, open-label study of nusinersen initiated in genetically diagnosed presymptomatic infants. Motor milestone achievement was assessed using date of first observed instance of achievement of WHO motor milestone (NURTURE) or HINE Section 2 or WHO motor milestones. (ENDEAR/SHINE). NURTURE 19 February 2020 and SHINE 27 Aug 2019 data are reported.
Results: Among NURTURE 2 SMN2 copy participants (n=15), 100% achieved sitting without support by age 1 year. 40% (42/105) of ENDEAR/SHINE participants have achieved sitting without support. Among ENDEAR/SHINE participants age 1.7–≤5.5 months at first dose (n=41), 37%, 10%, 10%, and 2% first achieved sitting alone by ages 1, 2, 3, and 4 years, respectively. Among ENDEAR/SHINE participants >5.5–≤8.0 months at first dose (n=40), 8%, 10%, 23%, and 3% first achieved sitting alone at the age cutoffs above. Among those age >8.0–≤23.0 months (n=24) at first dose, 1 participant (4%) first achieved sitting alone at age 4 years. 80% (12/15) of NURTURE 2 SMN2 copy participants have achieved walking alone: 60% (9/15) and 20% (3/15) by age 1 and 2 years, respectively. One ENDEAR/SHINE participant achieved walking alone by age 3 years (age at first dose: 1.7–≤5.5 months, n/N=1/41 [2%]). Motor function data (i.e., CHOP INTEND) by age at first dose groups will also be presented.
Conclusions: Results from these analyses demonstrate the importance of early initiation of nusinersen on motor milestone acquisition and motor function in individuals with SMA. Findings also highlight that clinical benefits can also be achieved when treatment is initiated at older ages.

Poster No. 030
Systemic Dose-Finding Study with AAV-Mediated γ-Sarcoglycan Gene Therapy for Treatment of Muscle Deficits in Limb-Girdle Muscular Dystrophy Type 2C Mice

YE SEO, AN KEMPTON, OC ROGERS, SH BAINE, S LEWIS, K ADEGBOYE, A HAILE, DA GRIFFIN, EL PETERSON, J RICHARDSON, ER POZSGAI, LR RODINO-KLAPAC
Sarepta Therapeutics, Inc., Cambridge, Massachusetts, USA

Objective: Limb-girdle muscular dystrophy type 2C (LGMD2C) results from γ-sarcoglycan (SGCG) gene mutations, and causes loss of functional protein. We tested the efficacy and safety of systemic gene transfer of SRP-9005 in SGCG-/- mice, and sought to establish minimum effective dose and proposed clinical dose for future study.
Methods: Self-complementary adeno-associated virus vector, scAAVrh74, containing a codon-optimized full-length human SGCG transgene, driven by the MHCK7 muscle-specific promoter, was systemically delivered via the tail vein to SGCG-/- mice that recapitulated the LGMD2C disease phenotype. 6 mice per cohort: saline-injected BL6 WT, saline-injected SGCG -/-, low dose: 4.63e12 vg/kg (8.94e10 vg total), mid dose: 1.85e13 vg/kg (3.63e11 vg total), high dose: 7.41e13 vg/kg (1.26e12 vg total). Endpoint analyses 12 weeks posttreatment: biomarker expression, transduction, histology, function, safety.
Results: Intravenous SRP-9005 administration to SGCG-/- mice with significant histopathology in muscle resulted in transgene expression throughout tibialis anterior (TA) limb, diaphragm, and heart across doses. SGCG-/- mice show absent or reduced sarcolemma expression of α-, β-, and δ-sarcoglycan (SGCA/SGCB/SGCD), components of the dystrophin-associated protein complex (DAPC). SRP-9005 increased SGCA/SGCB/SGCD subunit expression at sarcolemma in SGCG-/- mice, demonstrating dose-dependent restoration of DAPC proteins. Overall muscle pathology improved; central nuclei decreased. Fiber diameter increased in all, indicating normalized fiber size similar to WT fibers in TA, gastrocnemius, and triceps muscles. Functional improvement observed with significantly increased muscle strength (force

production) and resistance to contraction-induced injury in TA and diaphragm. SRP-9005 was associated with decreased CK. Liver enzymes normalized posttreatment.
Conclusions: AAV gene therapy demonstrated dose-dependent therapeutic benefit, widespread high-level protein expression, and histopathologic/functional improvements across doses. Dose-dependent response was seen in restoration of sarcoglycan complex proteins, indicating ability to restore additional DAPC proteins. The 7.41e13 vg/kg dose enabled the most robust SGCG expression and effective functional restoration, without adverse effects on non-target tissues.

Poster No. 031

SUNFISH Part 1: 24-month safety and exploratory outcomes of risdiplam (RG7916) treatment in patients with Type 2 or 3 spinal muscular atrophy (SMA)

JW DAY[1], G BARANELLO[2,3], O BOESPFLUG-TANGUY[4], S BORELL[5], N GOEMANS[6], J KIRSCHNER[5,7], R MASSON[3], MC PERA[8], L SERVAIS[9,10], S FUERST-RECKTENWALD[11], S FUHRER[12], M GERBER[13], K GORNI[14], H KLETZL[12], C MARTIN[15], WY YEUNG[15], E MERCURI[8]
[1]Department of Neurology, Stanford University, Palo Alto, CA, USA; [2]The Dubowitz Neuromuscular Centre, University College London, Great Ormond Street Institute of Child Health, London, UK; [3]Developmental Neurology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [4]I-Motion - Plateforme d'essais cliniques pédiatriques, Hôpital Armand Trousseau, Paris, France; [5]Department of Neuropediatrics and Muscle Disorders, Medical Center-University of Freiburg, Freiburg, Germany; [6]Neuromuscular Reference Centre, Department of Paediatrics and Child Neurology, University Hospitals Leuven, Leuven, Belgium; [7]Division of Neuropediatrics, University Hospital Bonn, Faculty of Medicine, Bonn, Germany; [8]Paediatric Neurology and Nemo Center, Catholic University and Policlinico Gemelli, Rome, Italy; [9]Reference Center for Neuromuscular Disease, Centre Hospitalier Régional de La Citadelle, Liège, Belgium; [10]MDUK Neuromuscular Centre, Department of Paediatrics, University of Oxford, Oxford, UK; [11]Pharma Development Neurology, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [12]Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel, Basel, Switzerland; [13]Pharma Development, Safety, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [14]PDMA Neuroscience and Rare Disease, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Roche Products Ltd, Welwyn Garden City, UK

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. A second gene, SMN2, produces low levels of functional SMN protein. Risdiplam (RG7916) is a centrally and peripherally distributed oral SMN2 pre-mRNA splicing modifier that increases the levels of functional SMN protein. SUNFISH (NCT02908685) is a multicenter, two-part, randomized, placebo-controlled, double-blind study of risdiplam (randomized 2:1, risdiplam:placebo) in patients with Type 2 or 3 SMA, aged 2–25 years. Part 1 (n=51) was a dose-selection study assessing the safety, tolerability and PK/PD of different risdiplam dose levels in patients with Type 2 or 3 SMA. SUNFISH Part 2 (n=180) is a confirmatory study assessing the safety and efficacy of the Part 1-selected dose level of risdiplam versus placebo in patients with Type 2 or 3 SMA. Despite not being designed to detect efficacy, exploratory 32-item Motor Function Measure (MFM32) results from Part 1 indicated that treatment with risdiplam led to improvements in motor function versus natural history after all patients were treated for a minimum of 12 months with the pivotal dose. Safety, tolerability and PK/PD data will be reported for the first time from all patients in Part 1 who have been treated with the pivotal dose of risdiplam for a minimum of 24 months. Updated Part 1 exploratory efficacy data, including motor outcome measures, will also be presented. The multinational SUNFISH study is the first positive placebo-controlled trial undertaken in a heterogeneous patient population with Type 2 or 3 SMA, aged 2–25 years. Part 1 and Part 2 of SUNFISH are ongoing globally.

Poster No. 032

Human pluripotent stem cells and artificial muscles for disease modelling of muscular dystrophies and therapy development

L PINTON[1,2], HB STEELE-STALLARD[1,2], D MOORE[1,2,3], S SARCAR[1], SM MAFFIOLETTI[1], M KHEDR[1,3], E NEGRONI[1,4], DJ WELLS[5], JM CUISSET[6], G BONNE[4], F MUNTONI[7], R PATANI[3,8], T ESCHENHAGEN[9], PS ZAMMIT[2], FS TEDESCO[1,3,7]
[1]Department of Cell and Developmental Biology, University College London, London, UK; [2]Randall Centre for Cell and Molecular Biophysics, King's College London, London, UK; [3]The Francis Crick Institute, London, UK; [4]Sorbonne Université, Inserm, Institut de Myologie, U974, Centre de Recherche en Myologie, Paris, France; [5]Department of Comparative Biomedical Sciences, Royal Veterinary College, London, UK; [6]Centre de Référence des maladies neuromusculaires, Service de Neuropédiatrie, Hôpital Roger Salengro, Lille, France; [7]Dubowitz Neuromuscular Centre, UCL GOS Institute of Child Health & Great Ormond Street Hospital for Children, London, UK; [8]UCL Queen Square Institute of Neurology, London, UK; [9]Department of Experimental Pharmacology and Toxicology, University Medical Center Hamburg Eppendorf, Hamburg, Germany

Objectives: Skeletal muscle is the most abundant human tissue and its regenerative capacity is compromised in severe incurable diseases such as muscular dystrophies. Therefore, developing reliable in vitro models of human skeletal muscle would be instrumental for investigating neuromuscular pathophysiology and developing novel therapies. However, current models are challenged by the limited lifespan and differentiation ability of biopsy-derived myoblasts and by the low-fidelity of standard cell cultures. To overcome these hurdles, we generated three-dimensional (3D) artificial skeletal muscle tissue from human induced pluripotent stem (iPS) cells, which have unlimited proliferative potential and controllable differentiation capacity.
Methods: Skeletal myogenic differentiation of iPS cells derived from children with Duchenne, limb-girdle and congenital muscular dystrophies was induced within biomaterials under tension to provide alignment of myofibres.
Results: 3D artificial muscles recapitulated structural and functional characteristics of human skeletal muscle. Furthermore, patient-specific artificial muscles containing key cellular constituents of normal skeletal muscle, including vascular cells and motoneurons were generated. This new model provided a platform to study pathological hallmarks of severe congenital muscular dystrophies caused by mutations in the LMNA gene, encoding the nuclear envelope protein LAMIN A/C (known as muscle laminopathies). Modeling in artificial muscles recapitulated nuclear shape abnormalities characteristic of laminopathies with higher fidelity than using standard cell cultures and identified nuclear elongation as a reproducible phenotypic readout. Moreover, we identified a patient with an LMNA mutation potentially amenable to new genetic therapies: we generated iPS cells and

noted elongated nuclei in the resulting myofibres, establishing the foundations for a drug screening platform for muscle laminopathies.
Conclusions: Engineering patient-specific iPS cell derivatives in a 3D environment can model cellular hallmarks of muscular dystrophies with high-fidelity, laying the foundation for future screening platforms and gene therapies for neuromuscular diseases.

Poster No. 033

Clinical and genetic spectrum of Charcot-Marie-Tooth Disease in East of England over a 10-year period

S MANIVANNAN[1], K COUSINS[1], G AMBEGAONKAR[1], J TAYLOR[2], S VELANDY[3], R HOVRATH[4], D KRISHNAKUMAR[1]
[1]Department of Paediatric Neurology, Addenbrooke's Hospital, Cambridge, UK; [2]Cambridge Community Services, Addenbrooke's Hospital, Cambridge, UK; [3]Psychological Medicine Service, Addenbrooke's Hospital, Cambridge, UK; [4]Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK

Aim: To describe disease burden and the genetic heterogeneity of Charcot-Marie-Tooth (CMT) disease in children referred to a tertiary neurology centre in the East of England.
Method: Retrospective electronic case note review was conducted over a 10-year period between 2009-2019. A total of 56 children aged between 2 and 17 years were identified.
Results: Age at diagnosis was 0 to 3 years (n=22), 4 to 6 years (n=12), 7 to 9 years (n=16). 36 were boys (64.3%) and 20 girls (35.7%). The reasons for referral were tip-toe walking (n=12); recurrent falls (n=14); positive family history (n=18); foot deformity (n=7); delayed walking (n=6); reduced visual acuity (n=1). All children underwent genetic testing. The commonest subtype was CMT1A (n=40), CMT2A (n=2), CMT2D (n=3); HNPP; CMT1B, CMT2C, CMT6, CMTX (n=1 each) and 5 children have no genetic diagnosis. Children with CMT1A and HNPP had duplication or deletion of PMP22 gene, respectively. Other mutations noted in our cohort were detected in the genes MPZ, MFN2, TRPV4 and GJB1. 8 children (14.3%) were found to have emotional health and neurodevelopmental difficulties. 3 each with intellectual disability and anxiety, 2 with ADHD and 2 with social-communication difficulties. Co-morbid mental health concerns were noted in 4 of the 8 children, 2 of which required psychotropic medications. 10 children had learning difficulties at diagnosis which remained stable. 17.9% had orthopaedic surgical interventions and 62.5% used orthotics. 53.4% had pain at last follow up requiring a combination of physiotherapy advice, medication and referral to orthopaedics.
Conclusion: This study describes the clinical characteristics and unidentified disease burden of psychological and behavioural problems in CMT. Pain and ambulatory difficulties required multidisciplinary input. Interventions to tackle these problems will improve the quality of life, chances of employment and independent life in future.

Poster No. 034

Systemic gene transfer with rAAVrh74.MHCK7.SGCB increased β-sarcoglycan expression in patients with limb girdle muscular dystrophy type 2E

LR RODINO-KLAPAC[1], ER POZSGAI[1], S LEWIS[1,2], DA GRIFFIN[1,2], AS MEADOWS[1,2], A NICHOLL[2], C NEASE[2], KJ LEHMAN[2], K CHURCH[2], NF MILLER[2], MA IAMMARINO[2], J RICHARDSON[1], LP LOWES[2], JR MENDELL[2,3]
[1]Sarepta Therapeutics, Inc, Cambridge, Massachusetts, USA; [2]Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio, USA; [3]Department of Pediatrics and Neurology, The Ohio State University, Columbus, Ohio, USA

Objective: Limb-girdle muscular dystrophy type 2E (LGMD2E), caused by a β-sarcoglycan (SGCB) gene mutation, is progressive and fatal. We present findings of a Phase I, escalating-dose gene transfer trial of 6 patients with LGMD2E who received rAAVrh74.MHCK7.SGCB (NCT03652259).
Methods: Patients: 4 to 15 years, SGCB mutation, >40% on 100-meter walk test. Cohort 1 (n=3) and Cohort 2 (n=3) received single IV infusions of 5x1013vg/kg rAAVrh74.MHCK7.SGCB and 2x1014vg/kg, respectively. Prednisone 1mg/kg/day was initiated 1d before infusion (30d-[Cohort 1] and 60d-[Cohort 2] taper). Primary endpoint: safety; secondary endpoint: SGCB expression 8 weeks posttreatment; other endpoints: CK decrease and functional endpoints.
Results: Immunohistochemistry Cohort 1: mean 51% SGCB-positive fibers expressing mean 47% intensity; mean 36.1% SGCB expression vs normal (western blot). Cohort 2: mean 72% SGCB-positive fibers expressing mean 73% intensity; mean 62.1% SGCB expression vs normal. Mean CK decreased from baseline by 72% at 1 year in Cohort 1, 89% at 90 days in Cohort 2. Functional improvements were observed in all Cohort 1 patients (North Star Assessment for Dysferlinopathy [NSAD], Time to Rise, 4-Stair Climb, 100-m timed test, 10-m Walk/Run); the mean change from baseline in NSAD at 1 year was 5.7 points. As of 03/25/2020, two Cohort 1 patients and one Cohort 2 patient had elevated liver enzymes, which returned to baseline levels following steroid treatment; one Cohort 2 patient had vomiting/dehydration (resolved).
Conclusions: Efficient transduction in skeletal muscle and robust β-sarcoglycan protein expression in all patients post-infusion with rAAVrh74.MHCK7.SGCB resulted in reductions in CK and functional improvements, suggesting improvement against disease-mediated muscle damage. Similar safety and tolerability profiles were observed in both cohorts.

Poster No. 035

Real-world treatment patterns and outcomes in patients with spinal muscular atrophy collected from the RESTORE registry

L SERVAIS[1], JW DAY[2], DC DE VIVO[3], J KIRSCHNER[4], F MUNTONI[5], PB SHIEH[6], E TIZZANO[7], S QUIJANO-ROY[8], K SAITO[9], O DABBOUS[10], A SHAH[10], FA ANDERSON[11], RS FINKEL[12]

[1]MDUK Oxford Neuromuscular Centre, University of Oxford, Oxford, UK; [2]Department of Neurology, Stanford University Medical Center, Stanford, CA, USA; [3]Departments of Neurology and Pediatrics, Columbia University Irving Medical Center, New York, NY, USA; [4]Clinic for Neuropediatrics and Muscle Disease, University Medical Center Freiburg, Freiburg, Germany; [5]Department of Developmental Neuroscience, University College London, London, UK; [6]Department of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [7]Department of Clinical and Molecular Genetics, Hospital Valle Hebron, Barcelona, Spain; [8]Garches Neuromuscular Reference Center (GNMH), APHP Raymond Poincare University Hospital (UVSQ Paris Saclay), Garches, France; [9]Institute of Medical Genetics, Tokyo Women's Medical University, Tokyo, Japan; [10]Novartis Gene Therapies, Bannockburn, IL, USA; [11]Center for Outcomes Research, Department of Surgery, University of Massachusetts Medical School, Worcester, MA, USA; [12]Translational Neuroscience Program, St Jude's Children's Research Hospital, Memphis, TN, USA

Objective: RESTORE is a prospective, multicentre, registry of patients with spinal muscular atrophy (SMA) designed to integrate and expand available real-world data, thus overcoming the limitations of existing single-product registries.
Methods: Data are incorporated from de novo clinical sites and the onasemnogene abeparvovec managed-access program. Target enrolment is ≥500 patients, with follow-up duration up to 15 years.
Results: As of 31 January 2020, data were available for 67 patients, all from de novo clinical sites in the United States; information on treatment regimens was available for 56 patients: onasemnogene abeparvovec alone (n=18), nusinersen alone (n=11), nusinersen after onasemnogene abeparvovec administration (n=2), nusinersen before onasemnogene abeparvovec administration (n=17), nusinersen both before and after onasemnogene abeparvovec administration (n=8). Ten patients had >1 CHOP INTEND score available for analysis and 8 (80%) had increased scores during the initial follow-up period. Adverse event (AE) data were reported for 39 of the 56 patients with known treatment regimens; 32 (82.1%) reported ≥1 AE; 15 (38.5%) reported ≥1 serious AE (6 [15.4%] related to treatment). We will present initial safety and efficacy findings by each treatment cohort. The RESTORE Registry continues to enroll new patients; as of 12 June 2020, the database comprises information from 104 patients and 41 active sites in the United States.
Conclusions: RESTORE provides extended real-world assessments of patient outcomes and SMA interventions. Most patients with >1 CHOP INTEND evaluation achieved higher scores over the initial follow-up period. Based on limited data available, AE experience of onasemnogene abeparvovec observed in the RESTORE Registry is consistent with experience in clinical trials for SMA; no new safety signals were identified among patients treated with onasemnogene abeparvovec or among those who switched treatments.

Poster No. 036

The utility of muscle MRI in the diagnosis of paediatric neuromuscular disorders

M TAYLOR[1], K PYSDEN[1], J KRAFT[2], AM CHILDS[1]

[1]Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK; [2]Department of Radiology, Leeds General Infirmary, Leeds, UK

Background: MRI is an important non-invasive tool in the diagnosis of specific neuromuscular disorders in adults. However its role in the diagnostic pathway for children with suspected NM disorders is less clear. The aim of this study was to evaluate the clinical utility of muscle MRI in a children's regional NM clinic.
Methods: Retrospective review of all muscle MR scans performed at Leeds Children's Hospital between 2008 and 2019. Findings were correlated with clinical features, other investigations including muscle biopsy and genetic analysis together with the final diagnostic outcome.
Results: 153 patients underwent a total of 169 MRI using standard T1 and STIR images of upper and lower limbs. Patients were subdivided into 3 categories: those with confirmed neuromuscular diagnosis (57), those with a probable neuromuscular diagnosis (35) and those unlikely to have a neuromuscular diagnosis (55). Four patients were lost to follow-up and two were not known to the children's neuromuscular service. Of the 57 with confirmed neuromuscular disorders 38 (66.7%) had evidence of muscle disease on MR whilst 19 (33.3%) had normal imaging. 17/38 had a recognizable pattern of muscle involvement that suggested a specific diagnosis, which was genetically confirmed in 11/17, with 6 having alternative genetic diagnoses. Of 35 patients with clinical features suggestive of probable neuromuscular disorder 24 (68.5%) had MR appearances consistent with NMD and 11 (31.5%) had normal scans. All 55 patients whose clinical picture was felt unlikely to be related to a neuromuscular disorder had normal imaging. The calculated sensitivity of muscle MRI for the diagnosis of neuromuscular disorders was 67.4%, with 100% specificity. Positive predictive value is 100% with a negative predictive value of 64.71%.
Conclusion: Muscle MR appears to be a useful part of the diagnostic pathway for children with suspected NM disorders with a high specificity and moderate sensitivity.

Poster No. 037

Would you invest in a SMA patient with only 1 copy of SMN2? What if you knew they could walk?

C BRYAN, DI MARCO, R MOCHRIE, SM MCKENZIE, RA HART, SJ BROWN, J DUNNE, S JOSEPH, IA HORROCKS

Glasgow Paediatric Neuromuscular Research Team, Glasgow, UK

Objectives: Spinal muscle atrophy (SMA) is a genetic neurodegenerative disorder that without treatment results in progressive muscle weakness and, in most forms, significantly shortened life expectancy. This occurs due to an absent Survival Motor Neurone Gene 1 which produces the SMN protein and therefore, patients rely on a reduced production by varying numbers of the SMN2 genes. A reasonable correlation is seen between limited numbers of SMN2 copies and SMA severity. It is still classified by phenotype and age of presentation but genotype may predict treatment response. Classically, Type 1 would have two copies, be unable to ever sit independently and life expectancy limited to around 2

years. Therefore, with the advent of Newborn National Screening programs (NBS) and the expectant huge costs of Gene Therapy (estimate £1.8m single treatment) would Trusts 'invest' in an SMA newborn with only 1 copy of SMN2? Here, we present a 4 year old girl, treated for over 3 years with Nusinersin (14 doses to date).

Case history: The patient was clinically diagnosed at 6.5 months following concerns surrounding development and lethargy while feeding. Genetics confirmed she had no copies of the SN1 gene and only 1 copy of SMN2 gene. Intrathecal Nusinersin was started at 8 months old with measurable developmental advances. Now, the patient is able to sit, crawl, walk with assistance of pelvic support and feed herself. Her latest R-CHOP score was 62/64. She has a normal sleep study and has no requirement for any breathing support.

Conclusions: It is felt this patient should be brought to the attention of fellow colleagues, considering the future implications of NBS. This case may assist physicians with decision making regarding treatment options where phenotypically the child may seem at odds with the genotype and therefore may benefit from aggressive early management.

Poster No. 038

RAINBOWFISH: A study of risdiplam (RG7916) in infants with presymptomatic spinal muscular atrophy (SMA)

L SERVAIS[1,2,3], E BERTINI[4], M AL-MUHAIZEA[5], L NELSON[6], A PRUFER[7], D VLODAVETS[8], Y WANG[9], E ZANOTELI[10], L BURKE[11], M EL-KHAIRI[11], K GORNI[12], H KLETZL[13], M GERBER[14], RS SCALCO[15], R FINKEL[16]

[1]I-Motion - Hôpital Armand Trousseau, Paris, France; [2]MDUK Oxford Neuromuscular Center, Department of Paediatrics, University of Oxford, Oxford, UK; [3]Division of Child Neurology, Centre de Références des Maladies Neuromusculaires, University Hospital Liege, Belgium; [4]Department of Neurosciences and Neurorehabilitation, Bambino Gesù Children's Research Hospital IRCCS, Rome, Italy; [5]Department of Neurosciences, King Faisal Specialist Hospital & Research Center, Riyadh, Kingdom of Saudi Arabia; [6]UT Southwestern Medical Center, Dallas, TX, USA; [7]Federal Uni Rio de Janeiro, Rio de Janeiro, Brazil; [8]Russian Children Neuromuscular Center, Veltischev Clinical Pediatric Research Institute of Pirogov, Moscow, Russia; [9]Children's Hospital of Fudan University, Shanghai, China; [10]Department of Neurology, Hospital das Clínicas, University of São Paulo, São Paulo, Brazil; [11]Roche Products Ltd., Welwyn Garden City, UK; [12]PDMA Neuroscience and Rare Disease, F. Hoffmann-La Roche Ltd., Basel, Switzerland; [13]Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel, Basel, Switzerland; [14]Pharma Development, Safety, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [15]Pharma Development Neurology, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Division of Neurology, Department of Pediatrics, Nemours Children's Hospital, Orlando, FL, USA

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. A second gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (RG7916) is a centrally and peripherally distributed oral SMN2 pre-mRNA splicing modifier that increases the levels of functional SMN protein. RAINBOWFISH (NCT03779334) is an open-label, single-arm, multicenter study to investigate efficacy, safety and pharmacokinetics (PK)/pharmacodynamics (PD) of risdiplam in infants with genetically diagnosed presymptomatic SMA. RAINBOWFISH is actively enrolling infants aged from birth to 6 weeks of age (at first dose), regardless of SMN2 copy number, who will receive risdiplam for 24 months, followed by a 36-month extension. Primary analyses will be conducted at 12 months of treatment in infants with two SMN2 copies and compound muscle action potential (CMAP) ≥1.5mV at baseline. The primary objective is to evaluate the efficacy of risdiplam, as determined by the proportion of infants sitting without support for 5 seconds after 12 months of treatment (as assessed by the Bayley Scales of Infant and Toddler Development, Third Edition). Secondary endpoints include the development of clinical symptoms, survival and permanent ventilation, achievement of motor milestones, motor function, growth measures, nutritional status, degree of innervation by CMAP, PK and respiratory effects by plethysmography. RAINBOWFISH will provide valuable information about presymptomatic administration of risdiplam alongside the ongoing FIREFISH (Type 1 SMA, NCT02913482), SUNFISH (Type 2/3 SMA, NCT02908685) and JEWELFISH (non-naïve patients with SMA, NCT03032172) studies. We will report the baseline demographics of enrolled infants and preliminary PK/PD data of risdiplam in a presymptomatic population of SMA. The RAINBOWFISH study is currently recruiting at selected sites worldwide.

Poster No. 039

An uncommon cause of episodic apnoea in twins

SSK DHULIPALA, A ISRANI, S SPINTY

Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Twin brothers were transferred to our centre for evaluation of hypotonia and episodic apnoea. They were born to non-consanguineous parents with unremarkable family history. They were born at 32 weeks of gestation. Perinatal period was remarkable for bilateral pleural effusions in both twins, requiring intercostal drainage. They were discharged on home oxygen for chronic lung disease. At 6 months of age, they developed episodes of apnoea. The episodes occurred during awake and sleep state, with saturations dipping to below 40, and accompanied by cyanosis. Examination revealed identical twins with marked dolicocephaly, oblong face, high arched palate, generalised hypotonia with paucity of antigravity movements in the limbs. Deep tendon reflexes were not elicitable. Other systemic examination was unremarkable. Diagnostic possibilities considered for apnoeas included exacerbations related to chronic lung disease, gastro-oesophageal reflux, fatigue related to neuromuscular condition – congenital myopathy, congenital myasthenia or congenital myotonic dystrophy. Creatine kinase levels were normal. Nerve conduction study and limited EMG did not reveal any significant abnormality. Genetic tests for spinal muscular atrophy, Prader –Willi syndrome and congenital myotonic dystrophy were negative. Echocardiography excluded structural cardiac abnormalities and cardiomyopathy. Muscle biopsy findings were supportive of diagnosis of centronuclear myopathy with type 1 fibre predominance and internalisation of nuclei with some centrally located nuclei. Exome sequencing revealed monozygotic twins having identical heterozygous pathogenic mutations in SPEG gene, associated with centronuclear myopathy type 5. Centronuclear myopathies (CNMs) are characterized by muscle weakness and increased numbers of central nuclei within myofibers. X-linked myotubular myopathy, the most common severe form of CNM, is caused by mutations in MTM1, encoding myotubularin (MTM1), a lipid phosphatase. Striated muscle preferentially expressed protein kinase (SPEG),

the product of SPEG complex locus (SPEG), is recently known to cause a CNM phenotype as a result of its interaction with MTM1.

Poster No. 040

Entonox administration in spinal muscular atrophy patients receiving intrathecal Nusinersen

DOR OROURKE[1], GM MURRAY[1], DOS OSHEA[2], LC COY[1], SB BRENNAN[2], DMCD MCDONALD[2]

[1]Childrens Health Ireland at Temple Street, Dublin, Ireland; [2]Childrens Health Ireland at Tallaght, Dublin, Ireland

Background: Intrathecal Nusinersen (Spinraza) is an intrathecally administered anti-sense oligonucleotide licensed for the treatment of SMA. In patients with SMA who have severe scoliosis, respiratory and bulbar failure and intrinsic anxiety procedural pain management can be challenging.
Aim: We examine the use of Entonox 50/50 in this patient group for the procedural pain management of this treatment.
Methods: Retrospective analysis of all SMA patients in our centre receiving Nusinersen over a 12 month period (Aug 2019–2020).
Results: Sixteen of 22 patients were identified who had received 42 doses. The mean age was 8.3 years (3–19 years). 15 patients had scoliosis with cobb angle >40 degrees. 15 patients required >12 hours/day of NIV. 4 patients had SMA type 1, 11 had SMA type 2 and 1 had SMA type 3. Total duration of time on Entonox was 16.4 minutes (10–27). Nusinersen was successfully administered in 41/42 doses. 14/42 doses required interventional radiology. 27/42 doses were administered in Day Ward procedural room. Crying or anxiety which was observed on 30/42 occasions immediately prior to procedure either stopped or improved on entonox in all cases. Dizziness, euphoria and giddiness were common side effects on entonox. No patients developed respiratory compromise or nausea. SaO2 was maintained over 96% in all patients for duration of entonox use. EMLA cream 5% was additionally used for all patients. Lidocaine 1% injection was administered for 14/42 doses. All patients were discharged home the same day.
Conclusion: Entonox is a safe, low cost, easy to use and well tolerated medication in the management of procedural pain in SMA patients receiving intrathecal Nusinersen. We suggest consideration of this analgesic in the procedural pain management of SMA patients receiving intrathecal Nusinersen.

Poster No. 041

Evaluating the efficacy of remotely administering and scoring the North Star Ambulatory Assessment (NSAA) in patients with Duchenne Muscular Dystrophy (DMD)

N EMERY, K STRACHAN, R KULSHRESTHA, T WILLIS

Neuromuscular Disease, Robert Jones & Agnes Hunt Orthopaedic Hospital, Shropshire, UK

Objective: The Sars-Cov-2 pandemic and subsequent Government 'lockdown' has meant that boys with Duchenne Muscular Dystrophy (DMD) have not being seen in clinic for assessments and their North Star Ambulatory Assessment (NSAA) not administered. The NSAA is a validated and reliable 17-item functional rating scale and widely used to assess motor function in DMD boys. The standards of care recommend that DMD boys are seen every 6 months to assess function using the NSAA. The aim is to investigate whether the NSAA could be used to accurately and reliably score ambulant boys with DMD by video assessment.
Methods: Ten ambulant DMD boys were selected from electronic hospital records at the Robert Jones & Agnes Hunt Orthopaedic Hospital (RJAH). Two Physiotherapists scored the DMD boys NSAA independently. The video scores were compared to the 2 previous face-to-face NSAA scores.
Results: Mean scores (SD) for NSAA face-to-face visit one were: 22.6 (4.19); visit two 21.8 (5.3). The two Physiotherapist video mean NSAA scores were 20.6 (5.66); Physiotherapist 1 and 20.6 (6.53) Physiotherapist 2. Decline in score from face-to-face visit one (−12 months) to video assessment was 2.1 (3.09). This is consistent with the results of Mazzone et al (2011) where a mean decline in 12 months of 2.2 (3.7) was observed in 106 DMD boys.
Conclusion: The results from the study suggest that video NSAA is accurate and reliable. However further studies with a larger cohort would need to be conducted to confirm these findings.

Poster No. 042

Upper airway obstruction in a profoundly hypotonic neonate due to parapharyngeal neuroglial heterotopia – a case report

J THOMPSON[2], E HOGG[1], S DE[1], E HAMOUDA[3], A FELTON[4], S DHULIPALA[2], K VYHNALKOVA[2], S SPINTY[2]

[1]ENT Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [2]Neuromuscular Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [3]Radiology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [4]Speech and Language Therapy, Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Introduction: A male term baby with unremarkable pre-, peri- and postnatal history was transferred to a tertiary paediatric ENT unit at 72 hours with noisy breathing and desaturations. Flexible nasendoscopy revealed shortened aryepiglottic folds and findings consistent with reflux. Stertor improved with simple airway manoeuvres. He required high-flow oxygen, a nasopharyngeal airway and subsequently continuous positive airway pressure to maintain saturations. At 5 weeks old he developed severe hypotonia and tongue fasciculations.
Investigations: Electromyogram and nerve conduction study (EMG/NCS) were supportive of anterior horn cell disease. Repeat EMG/NCS at 7 weeks showed minimal evidence of ongoing denervation but evidence of previous denervation and collateral reinnervation within the tongue. Genetic analysis for 5q related Spinal Muscular Atrophy (SMA) was negative. CT/MRI of brain and neck demonstrated a right parapharyngeal complex solid, cystic mass with multiple internal stations, no communication with intracranial structures, compressing and narrowing the oropharyngeal airway. Examination under anaesthesia confirmed a large mass arising from the lateral nasopharyngeal wall, extending across the midline filling the nasopharynx involving the right side of the soft palate, splinting and pushing it inferiorly. Biopsy confirmed neuroglial heterotropia.
Management: Debulking of the lesion allowed self-ventilation in air. Imaging confirmed interval increase of the lesion requiring further debulking at 3 weeks post-operatively, after representation

with upper airway obstruction. His muscle tone improved and by 16 weeks old he was able to roll over.
Discussion: The diagnosis of neuroglial heterotropia is rare and was delayed, likely overshadowed initially by the potential diagnosis of SMA. The cause of the baby's initial profound hypotonia and EMG/NCS findings remain unexplained. No link between neuroglial heterotropia and his neurological presentation was identified. Potential intermittent compression of parts of the hypoglossal nerve may account for tongue fasciculation. Compression of other neuronal structures does not seem a likely explanation for severe hypotonia.

Poster No. 043
Novel case of POMGnT1-associated cardiomyopathy

ER WHITEHOUSE, D RAM, MI HUGHES
Paediatric Neurology, Royal Manchester Children's Hospital, Manchester, UK

Introduction: Dystroglycanopathies are rarely associated with cardiac complications. To our knowledge, this is the first case of POMGnT1 muscle-eye-brain disease associated with fatal cardiomyopathy.
Case: We describe a 15 year old boy who was born to consanguineous Asian parents. He initially presented at 4 months old with hypotonia, poor visual function with dysplastic optic discs and elevated CK (>2000 units/L). MR imaging showed partial lissencephaly with brainstem and corpus callosum hypoplasia and abnormal white matter signal. Subsequent genetic testing found pathogenic homozygous variants in POMGnT1. Routine cardiac surveillance was not organised given lack of association between POMGnT1 dystroglycanopathy and cardiac disease. Although he had epilepsy, severe learning difficulty and was non-ambulant, he remained clinically stable until 15 years old when he presented with increased work of breathing. A chest X-ray demonstrated cardiomegaly and pulmonary oedema. Echocardiogram confirmed the presence of dilated cardiomyopathy and he was commenced on diuretics and inotropic support; subsequently an ACE inhibitor was added but a beta-blocker was not tolerated. He remained asymptomatic for a few months but deteriorated further in the setting of an intercurrent illness. In accordance with family's wishes, care was reoriented towards a palliative approach and he subsequently died at home.
Discussion: Cardiac involvement in children with dystroglycanopathies remains poorly described in literature. Dilated cardiomyopathy is most commonly described in FKRP and FKTN (fukutin) mutations, but very rarely associated with other dystroglycanopathies. POMT1 and POMT2 mutations have been very rarely associated with cardiac disease. To our knowledge, there are no publications of POMGnT1 mutations associated with cardiomyopathy. Thus, our case expands the clinical spectrum of POMGnT1 dystroglycanopathy to include cardiac disease.
Conclusion: We recommend cardiac surveillance in all children with dystroglycanopathies, including those with POMGnT1 mutations. Despite its rare association, early diagnosis could potentially lead to better outcomes in some of these children.

Poster No. 044
A novel missense variant in the FHL-1 gene in a patient with Emery Dreifuss muscular dystrophy and biliary atresia

A SYED[1], A DALLOSSO[2], A MAJUMDAR[1]
[1]Department of Paediatric Neurology, Bristol Children's Hospital, University Hospital NHS Foundation Trust, Bristol, UK; [2]Bristol Genetics Laboratory, Pathology Sciences, Southmead Hospital, North Bristol Trust, Bristol, UK

Objective: To describe a novel FHL-1 (Four-and-a-Half LIM - 1) gene variant mutation causing Emery-Dreifuss Muscular Dystrophy (EDMD) in a 10 year old female.
Methods and Results: FHL1 is an X-linked gene (on Xq26.3) with multiple overlapping splice isoforms, highly expressed in skeletal and cardiac muscle, with functions in myoblast differentiation and sarcomere assembly. Truncating or missense pathogenic variants tend to be located in the highly conserved Zinc-finger LIM domains. Mutations in FHL-1 are associated with several clinically distinct myopathies. We describe the EDMD phenotype which is the clinical triad of muscle weakness, contractures and cardiomyopathy. Our patient presented at 7 years of age with marked shoulder, neck and pelvic girdle weaknesss and wasting, scapular winging, and spinal rigidity. Over the years, she developed progressive muscle weakness, swallowing difficulties, proximal joint contractures, distal laxity in joints and lipodystrophy. Her phenotype was typical of X-linked EDMD, with additional unusual features of biliary atresia, urinary incontinence and autistic spectrum disorder. Her muscle biopsy showed myopathic and neurogenic changes. Nerve conduction studies, MRI head and spine and echocardiogram were all normal.
Conclusions: A novel missense variant was identified at c.530A>C p.(Gln177Pro) within FHL1 gene outside of "hotspot" region where multiple previous pathogenic variants have been identified. This was a de novo heterozygous variant; absent in both parents and controls (using gnomAD database). Glutamine 177 is highly conserved and multiple lines of computational evidence support a deleterious effect on the gene product with its substitution to proline and fits patient's phenotype clinically with an FHL1-opathy. At the same locus (Xq26.3) the ZIC3 gene encodes nuclear proteins thought to function as transcription factors in early stages of left-right body axis formation. Variations here are associated with biliary atresia but this case does not have any other features associated with ZIC3.

Poster No. 045
Neuromuscular presentations of Friedreich's Ataxia in childhood

L D'ARGENZIO[1], MA FERNANDEZ-GARCIA[1], M LAZARO[2], E WRAIGE[1], H JUNGBLUTH[1,3,4]
[1]Department of Paediatric Neurology, Neuromuscular Service, Evelina Children's Hospital, London, UK; [2]Department of Neurophysiology, Guy's and St Thomas' Hospital NHS Foundation Trust, London, UK; [3]Muscle Signalling Section, Randall Division for Cell and Molecular Biophysics, King's College, London, UK; [4]Department of Basic and Clinical Neuroscience, King's College, IoPPN, London, UK

Background: Friedreich's Ataxia (FA) is a rare multisystemic autosomal recessive disorder that manifests during childhood with progressive ataxia, spasticity, cognitive impairment as well as visual impairment and hearing loss. In atypical cases, main

features may be absent at the onset while other secondary signs and symptoms could be more prominent.
Objective: Here we report four new cases of children with FA, who were referred to our tertiary neurological centre because of motor developmental delay associated with pes cavus (in three cases) and early onset scoliosis (in one case).
Results: Children presented between 4 and 8.5 years of age and were followed for an average of 4 years (0.5–10 years) in our clinic. They developed marked sensory loss but had intact motor strength in the lower limbs. An associated sensory ataxia was noticeable at the time of evaluation. In all cases, nerve conduction studies confirmed absent sensory potentials with normal motor conduction velocities. Further signs/symptoms developed after the diagnosis of FA was confirmed by genetic testing. Two cases developed spinal scoliosis and hypertrophic cardiomyopathy was also reported in three children.
Conclusions: Diagnosis of FA in atypical cases mimicking genetic neuropathies may prove challenging and could be easily missed without appropriate targeted genetic testing. FA should be suspected in children with pes cavus and early-onset scoliosis as well as with severely affected sensory but intact motor nerve conduction velocities at electrophysiological studies.

Poster No. 046
JEWELFISH: Safety and pharmacodynamic data in non-naïve patients with spinal muscular atrophy receiving treatment with risdiplam (RG7916)

CA CHIRIBOGA[1], C BRUNO[2], T DUONG[3], D FISCHER[4], J KIRSCHNER[4,5], E MERCURI[6], M GERBER[7], K GORNI[8], H KLETZL[9], T MCIVER[10], R SCALCO[11], F WARREN[10], M SCOTO[12]

[1]Department of Neurology, Columbia University Medical Center, New York, NY, USA; [2]Translational and Experimental Myology Centre, Istituto Giannina Gaslini, Genoa, Italy; [3]Department of Neurology, Stanford University, Palo Alto, CA, USA; [4]Division of Neuropediatrics, University Children's Hospital Basel, University of Basel, Basel, Switzerland; [5]Department of Neuropediatrics and Muscle Disorders, Medical Center-University of Freiburg, Freiburg, Germany; [6]Paediatric Neurology and Nemo Center, Catholic University and Policlinico Gemelli, Rome, Italy; [7]Pharma Development, Safety, F. Hoffmann-La Roche Ltd., Basel, Switzerland; [8]PDMA Neuroscience and Rare Disease, F. Hoffmann-La Roche Ltd., Basel, Switzerland; [9]Roche Pharmaceutical Research and Early Development, Roche Innovation Center Basel, Basel, Switzerland; [10]Roche Products Ltd., Welwyn Garden City, UK; [11]Pharma Development Neurology, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [12]The Dubowitz Neuromuscular Centre, UCL Great Ormond Street Institute of Child Health, London, UK

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. A second SMN gene, SMN2, produces only low levels of functional SMN protein. Risdiplam (RG7916) is a centrally and peripherally distributed oral SMN2 pre-mRNA splicing modifier that increases the levels of functional SMN protein. JEWELFISH (NCT03032172) is a multicenter, open-label study of daily oral risdiplam in non-naïve patients with SMA, aged 6 months to 60 years. JEWELFISH participants previously received RG7800 (RO6885247), nusinersen (SPINRAZA®), olesoxime or onasemnogene abeparvovec-xioi (ZOLGENSMA®). JEWELFISH (N=174) assesses the safety, tolerability and pharmacokinetics/pharmacodynamics (PK/PD) relationship of risdiplam. We have previously presented safety data from 45 patients with SMA (data-cut: 28th June 2019) who received risdiplam for up to 28.9 months (nine patients previously received RG7800, 24 patients received nusinersen and 12 patients received olesoxime). No drug-related safety findings leading to withdrawal were reported and there have been no treatment-related safety findings leading to withdrawal in any risdiplam trial (data-cut: 28th June 2019). In an earlier analysis of SMN protein in whole blood from patients in JEWELFISH, while patient numbers were limited (n=18), the magnitude of SMN protein increase (>2-fold) was comparable to that in SUNFISH Part 1 (NCT02908685) in patients with Types 2 and 3 SMA who had not previously received an SMN2-targeting therapy. We will present updated data on safety and PK/PD from patients within the JEWELFISH study, including new patients, and reasons for discontinuing previous treatment regimens. The JEWELFISH study is ongoing in sites across Europe and the US.

Poster No. 047
Patient satisfaction of video consultations in paediatric patients attending a regional neuromuscular clinic

KL STEVENSON, G NICFHIRLEINN, S TIRUPATHI
Royal Belfast Hospital for Sick Children, Belfast, UK

Objective: The impact of the Covid-19 pandemic has been far reaching. Preparing for the wave of acutely unwell patients whilst trying to maintain current patient care is a difficult balance. The paediatric neuromuscular team adapted by providing patient reviews via Microsoft Teams. This survey looks at caregivers views of the teleconferencing system provided and potential pitfalls that may arise in patient care.
Method: Email questionnaires were sent out to all of the parents/caregivers who attended the neuromuscular clinic via Microsoft Teams from May 2020 to July 2020.
Results: Thirty six were invited for the Microsoft Teams consultations. Three families were unable to use the Microsoft teams due to technical difficulties. Eight out of 33 (24%) attendees responded to the questionnaire. 100% (8/8) reported the technology as "easy to use". 75% (6/8) were "very satisfied" and 25% (2/8) "satisfied" with the service. 88% (7/8) reported less travel, 50% (4/8) reported less waiting and 25% (2/8) reported greater comfort for their child. Negatives included not having access to physical examination (which was cited by 25% (2/8) of respondents).
Conclusions: Covid-19 has plunged the healthcare service into availing technology to provide a service for patients. Whilst it is likely that face to face appointments will be required at some stage there is increasing evidence that the majority of clinic assessments can be made via telemedicine and that families and caregivers find this convenient and easy to access with the bonus of saving time, money and hassle.

Poster No. 048

Topiramate as adjunctive treatment for weight management in Duchenne muscular dystrophy

J THOMPSON[1], S DHULIPALA[1], K VYHNALKOVA[1], C GREAVES [2], C MEEHAN[2], T HENDERSON[1], S SPINTY[1]
[1]Neuromuscular Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [2]Dietetics, Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Background: Duchenne muscular dystrophy (DMD) is a multi-system, life-limiting, X-linked recessive disorder. Long term glucocorticoids are a well-established treatment for DMD and have been proven to prolong ambulation, preserve upper limb, respiratory and cardiac function. DMD patients have an increased risk of obesity in early life due to a variety of factors including steroids and reduced physical activity. As well as the general risks associated with childhood obesity (obstructive sleep apnoea, hypertension, psychosocial impact), obesity in DMD is likely to further impair mobility, increase falls and fractures and increase the risk of diabetes associated with steroid use. Migraines occur in 5% of school aged children in the UK. NICE guidelines for prophylactic management of migraines in 12 years and older recommends propranolol or topiramate as first line therapy. Topiramate is licenced to treat childhood epilepsy for a number of years. Among described side effects of topiramate are nasal congestion, depression, paraesthesias, somnolence, dizziness, nausea, diarrhoea and weight loss.
Method: Three patients under our care affected by DMD presented with frequent migrainous headaches. All three patients plotted over the 75th centile for their weight, significantly out of proportion for their height. All were formally assessed and received dietetic advice from our neuromuscular dieticians. They were titrated to a low or medium dose of topiramate for migraine management.
Results: All three patients' migraines significantly improved or resolved. Patients are being monitored for side effects which have been minimal and resolved with dose alterations. At this time, all three patients are showing a trend of reduction in weight for their age.
Conclusion: Topiramate might be a potential adjunctive treatment for obesity management in individuals affected by DMD and appears well tolerated. A formal study to investigate this further is in set up at Alder Hey Children's Hospital.

Poster No. 049

Zellwegers an important cause of neonatal hypotonia

K KALRA, AV ISRANI
Alder Hey Children's Hospital, Liverpool, UK

A 2 week old boy presented with generalized hypotonia, poor swallow, seizures and a deranged LFT. He was first child of non-consanguineous parents. With an uneventful antenatal history born at 42+5 weeks and a birth weight of 2.5kg, meconium stained vaginal delivery, floppy needed some respiratory support. There was no evidence of sepsis or hypoxic ischaemic encephalopathy. Examination showed dysmorphological features - large anterior and posterior fontanelle, depressed nasal bridge, epicanthal folds, bell shaped chest, and pes cavus with both the testes high in scrotal sac. Neurological examination showed reduced power with some antigravity movements and profound hypotonia with absent reflexes. Rest of the systemic examination was normal. At 2 weeks he continued to have seizures confirmed on EEG. Thereafter, developed shallow respirations with desaturations needing non-invasive ventilation (NIV). MRI brain reported bilateral perisylvian polymicrogyria. With this background peroxisomal biogenesis disorder (Zellweger syndrome) was confirmed with markedly raised VLCFA and phytanic acid levels. Also, USG abdomen showed renal cysts and x rays showed chondrodysplasia punctata in both patellas. Subsequently whole exome sequencing showed homozygous mutation of PEX 6 genes with biparental inheritance. Zellweger syndrome (ZS, an autosomal recessive disorder) belongs to a group of four related diseases called peroxisome biogenesis disorders (PBD). PBD occur 1 in 50,000, caused by mutations in one of the 13 PEX genes encoding peroxins. ZS is most severe within the spectrum leading to death within first year of life. Patients present in the neonatal period with distinctive facial stigmata, pronounced hypotonia, poor feeding, hepatic dysfunction, seizures and boney abnormalities. ZS is confirmed with elevated levels of very long chain fatty acids (VLCFA) due to functionally incompetent peroxisomes. Here we want to highlight how rational clinical decision making with the help of simple tests can lead to diagnosis, helping in timely and appropriate care.

Poster No. 050

The differential diagnosis of childhood neurodegenerative disease according to age and ethnic group.

CM VERITY, SE BAKER, PJ MAUNDER, AM WINSTONE
Addenbrooke's Hospital, Cambridge, UK

Objective: To report the differential diagnosis according to age and ethnic group in children with progressive intellectual and neurological deterioration (PIND) notified to this UK-wide study.
Methods: Since 1997 the study has searched for variant Creutzfeldt-Jakob disease (vCJD) in children by performing prospective epidemiological surveillance of those aged less than 16 years with PIND.
Results: From May 1997 to October 2019, 2255 children meeting the criteria for PIND had been notified, of whom 2008 (males 1085, females 923) had underlying diagnoses. There were over 220 different diseases, including 6 cases of vCJD. The numbers presenting in four age groups were: <1 year: 805 (40%), 1 to 4 years inclusive: 825 (41%), 5 to 9 years inclusive: 264 (13%), 10 to 15 years inclusive: 114 (6%). The two largest ethnic groups were White and Pakistani (58.2% and 17% of diagnosed cases). The most common diseases in these two ethnic groups were determined for the four age groups. The distribution of diseases varied with age but there were similarities between White and Pakistani children. For example in those <1 year old, 6 of the 11 commonest diagnoses in White children were among the 11 commonest diagnoses in Pakistani children. This will be illustrated by showing the commonest diagnoses in two age groups: <1 year and 10 to 15 years.
Conclusions: This is a unique guide to diseases causing childhood PIND, which are rare (circa 0.1/1000 live births), but a source of great concern to parents and health professionals. Most are genetically determined, presenting in early childhood (81% before age

5 years). There were considerable differences between the four age groups but similarities between ethnic groups. The hope is that this analysis of the aetiology of PIND will help paediatricians when investigating children with neurodegenerative diseases. Meanwhile the PIND Study provides the only systematic surveillance for vCJD in UK children.

Poster No. 051

The spectrum of paediatric neurosurgical interventions in paediatric NF1

K VRAKA[1], D VARTHALITIS[2], L LUNT[3], HUPTON E[3], J EELLOO[3], I KAMALY[2], S WEST[1], G VASSALLO[1]

[1]Paediatric Neurology Department, Royal Manchester Children's Hospital, Manchester, UK; [2]Paediatric Neurosurgical Department, Royal Manchester Children's Hospital, Manchester UK; [3]Genetics, Nationally NHS Commissioned NF1 Service, UK

Objective: The aim of this study is to present the spectrum of Neurosurgical Interventions required in children with Neurofibromatosis type 1 (NF1) in North England.

Material and methods: The NHS Nationally Commissioned Highly Specialised Service (HSS) for NF1 patients in Manchester serves NF1 patients in the North of England. Currently our service looks after 351 children (F=159 M=192) aged 0 to 18 years. A retrospective review of their neuroimaging, presentation and neurosurgical interventions needed was conducted, using our NF1 clinical database.

Results: 34/351 (10%) patients (15:19 males:females), with median age 7.85y [0.25y, 17y] underwent 43 neurosurgical interventions: 12 (28%) scoliosis repairs, 6 (14%) pial synangioses, 8 (18%) endoscopic third ventriculostomies (ETV), 5 (12%) VP or VA shunt insertions, 3 (7%) spinal cord decompressions, 3 (7%) foramen magnum decompressions and 6 (14%) had tumour resections. ETVs were performed to treat obstructive hydrocephalus secondary to brainstem gliomas (4/8), bulkiness of the tectal plate (1/8), web in the aqueduct (1/8) and primary aqueduct stenosis (2/8). 5/34 patients (15%) were asymptomatic. In the Moya Moya group: 1 was asymptomatic, 3 had Transient Ischaemic Attacks, 1 had haemorrhagic stroke, 1 had worsening speech and clumsiness. All those patients underwent pial synangiosis, based on their progression of radiological findings (i.e. Ivy sign, low perfusion, narrowing of ICA/MCA) and severity of clinical symptomatology. All of them had a good post-operative outcome. In the Chiari malformation group, requiring foramen magnum decompression, 2 were asymptomatic and 1 presented with nausea, vomiting and seizures with obstructive hydrocephalus. Everyone who underwent spinal cord decompression had neurological symptoms from cervical cord compression.

Conclusion: Neurosurgical intervention is rarely required in children with NF1. In our population, the most common intervention was scoliosis repair. A small proportion of children requiring intervention were asymptomatic and the decision for intervention were guided by neuroradiological progression and MDT discussion.

Poster No. 052

Interim results from phase 2/3 (ALD-102) and phase 3 (ALD-104) studies of elivaldogene autotemcel (Lenti-D) gene therapy for the treatment of cerebral adrenoleukodystrophy

P GISSEN[1], FS EICHLER[2], CN DUNCAN[3], PJ ORCHARD[4], SN DE OLIVEIRA[5], AJ THRASHER[1], C SEVIN[6], HM AMARTINO[7], N SMITH[8], J-S KÜHL[9], D KENNEY-JUNG[3], R CHIESA[5], J-H DALLE[10], J XU[11], AC DIETZ[11], E MCNEIL[11], P AUBOURG[12], DA WILLIAMS[13]

[1]UCL Great Ormond Street Hospital Institute of Child Health and Great Ormond Street Hospital NHS Trust, London, UK; [2]Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA; [3]Boston Children's Hospital and Dana-Farber Cancer Institute, Boston, MA, USA; [4]University of Minnesota Children's Hospital, Minneapolis, MN, USA; [5]University of California, Los Angeles, Los Angeles, CA, USA; [6]Hôpital Universitaire Hôpital Bicêtre-Hôpitaux Universitaires Paris Sud, Paris, France; [7]Medeos, Buenos Aires, Argentina; [8]Women's and Children's Hospital, Adelaide, Australia; [9]Department of Pediatric Hematology/Oncology/Hemostaseology, University Hospital Leipzig, Leipzig, Germany; [10]Robert-Debre Hospital, GHU Nord-Université de Paris, France; [11]bluebird bio, Inc., Cambridge, MA, USA; [12]INSERM & Hôpital Bicêtre, Paris, France; [13]Dana-Farber & Boston Children's Cancer and Blood Disorders Center, Harvard Medical School & Harvard Stem Cell Institute, Boston, USA

Objective: Preliminary results from ALD-102 study of elivaldogene autotemcel (eli-cel; Lenti-D gene therapy) showed that 88% patients with cerebral adrenoleukodystrophy (CALD) met the primary endpoint of survival free of major functional disabilities (MFD) at 24 months. Here, we report updated results for the fully enrolled ALD-102 and preliminary data from study ALD-104 investigating an alternative myeloablative protocol that utilizes busulfan/fludarabine instead of busulfan/cyclophosphamide.

Methods: Post-conditioning, patients with CALD (male, ≤17 years) received eli-cel (autologous CD34+ cells transduced with Lenti-D lentiviral vector encoding ABCD1 cDNA). After ALD-102/ALD-104 (2 years), monitoring continues for additional 13 years in LTF-304. Data are median (min–max).

Results: As of January 2020, 32 eli-cel-treated patients in ALD-102/LTF-304 had 30.0 (9.1–70.7) months follow-up. The primary efficacy endpoint was met in 20/23 (87%) evaluable patients; 2 withdrew and 1 died. Nine additional patients continue to be followed in ALD-102 (maximum follow-up 22.1 months) and 20 are enrolled in LTF-304; all but one show CALD stabilization. As of February 2020, 13 patients were treated in ALD-104 with 6.1 (2.2–10.3) months follow-up. Two patients had delayed hematologic reconstitution; 13 achieved neutrophil and 12/13 platelet engraftment, to date. In both studies, adverse events were generally consistent with myeloablation; no graft failure or graft-versus-host-disease occurred. One patient in ALD-102 had benign clonal expansion without clinical consequences at last visit (month 60).

Conclusions: Eli-cel continues to show a favorable benefit/risk profile with up to 71 months follow-up in ALD-102/LTF-304. Evolving data from ALD-102 and ALD-104 will allow further insights into the clinical impact of eli-cel in CALD.

Poster No. 053

Leukoencephalopathy with calcifications and cysts: genetic and phenotypic spectrum

YJ CROW

Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, UK

Biallelic mutations in SNORD118, encoding the small nucleolar RNA U8, cause leukoencephalopathy with calcifications and cysts (LCC). Given the difficulty in interpreting the functional consequences of variants in non-protein encoding genes, and the high allelic polymorphism across SNORD118 in controls, we set out to provide a description of the molecular pathology and clinical spectrum observed in a cohort of patients with LCC. We identified 64 affected individuals from 56 families. Age at presentation varied from 3 weeks to 67 years, with disease onset after age 40 years in eight patients. Ten patients had died. We recorded 44 distinct, likely pathogenic, variants in SNORD118. Fifty two of 56 probands were compound heterozygotes, with parental consanguinity reported in only three families. Forty nine of 56 probands were either heterozygous (46) or homozygous (three) for a mutation involving one of seven nucleotides that facilitate a novel intramolecular interaction between the 5' end and 3' extension of precursor-U8. There was no obvious genotype-phenotype correlation to explain the marked variability in age at onset. Complementing recently published functional analyses in a zebrafish model, these data suggest that LCC most often occurs due to combinatorial severe and milder mutations, with the latter mostly affecting 3' end processing of precursor-U8.

Poster No. 054

Genetic and phenotypic spectrum associated with MDA5 gain-of-function

YJ CROW

Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, UK

Background: MDA5 gain-of-function has been reported as a cause of a type I interferonopathy encompassing a spectrum of autoinflammatory phenotypes including Aicardi-Goutières syndrome and Singleton Merten syndrome.
Objectives: To describe the molecular, clinical and interferon status of a cohort of individuals with pathogenic heterozygous mutations in IFIH1.
Methods: Patients were ascertained through a European and North American collaboration. Sequencing data were considered along with ex vivo and in vitro assessments of interferon signalling status and structural modelling.
Results: We identified 74 individuals from 51 families segregating a total of 27 likely pathogenic mutations in IFIH1. Ten adult individuals, 13.5% of all mutation carriers, were clinically asymptomatic (with seven of these aged over 50 years). All mutations were associated with enhanced type I interferon signalling, including six variants (22%) which were predicted as benign according to multiple in silico pathogenicity programs. The identified mutations cluster close to the ATP binding region of the protein.
Conclusions: Our data confirm variable expression and non-penetrance as important characteristics of the IFIH1 genotype, a consistent association with enhanced type I interferon signalling, and a common mutational mechanism involving increased RNA binding affinity or decreased efficiency of ATP hydrolysis and filament disassembly rate.

Poster No. 055

ATP1A3-related disorders within the DDD cohort. Are we underestimating the developmental phenotype?

K VEZYROGLOU[1,4], RS AKILAPA[2], DDD STUDY GROUP[3], M KURIAN[1,4], JH CROSS[1,4], M BALASUBRAMANIAN[2]

[1]Developmental Neurosciences, UCL Institute of Child Health, London, UK; [2]Sheffield Clinical Genetics Service, Sheffield Children's NHS Foundation Trust, Sheffield, UK; [3]DDD Study, Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK; [4]Neurology, Great Ormond Street Hospital for Children, London, UK

Objective: The ATP1A3 gene is associated with a broad spectrum of predominantly neurological disorders, including the defined phenotypes of alternating hemiplegia of childhood (AHC), rapid-onset dystonia parkinsonism (RDP) and CAPOS. The Deciphering Developmental Disorders (DDD) study uses whole exome sequencing to link previously undiagnosed phenotypes to known and novel genotypes. We expand on clinical features of individuals diagnosed with pathogenic variants within the DDD network.
Methods: We harnessed data from the DDD-Decipher database for variants in ATP1A3. Clinicians were contacted to provide detailed phenotypic information. Participants with pathogenic and likely pathogenic ATP1A3 variants were included in this study.
Results: Eighteen patients with a previously undiagnosed neurological phenotype were found to carry likely pathogenic ATP1A3 variants. Four variants have previously been published, 14 are novel. Mean age was 15.9 years (SD=10.4) with mean age of disease onset 5.9 months (SD=6). Thirteen (72.2%) patients were female. Initial concern was either developmental delay (n=8, 44.4%) or seizures (n=6, 33.3%) in most. All patients experienced at least one type of paroxysmal events: hemiplegic events (6; 33.3%), dystonic events (9; 50%), abnormal eye movements (9; 50%), apneic episodes (3; 16.7%), autonomic episodes (5; 27.8%) and epileptic seizures (10; 55.6%). Permanent neurological features were common including microcephaly (6; 33.3%), ataxia (10; 55.6%), dystonia (7; 38.9%) and hypotonia (7; 38.9%). All patients had cognitive impairment (21.4% mild, 28.6% moderate, 50% severe). Behavioural difficulties were reported in 11 (61.1%) patients; ASD (6; 33.3%), ADHD (4; 22.2%) and childhood onset schizophrenia (1; 5.5%).
Conclusions: The clinical features identified in this study have previously been reported in ATP1A3-related disease. However, in most patients reported here the constellation of features did not meet diagnostic criteria for any of the recognized ATP1A3-related clinical syndromes and "hallmarks" of the disease, such as hemiplegic events, were often absent. The broader inclusion of ATP1A3 in panel investigations of patients, especially with developmental or behavioural phenotypes would aid earlier diagnosis.

Poster No. 056

Differential expression of interferon alpha protein provides clues to tissue specificity across type I interferonopathies

YJ CROW

Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, UK

Whilst, by definition, up-regulation of type I interferon (IFN) signalling is a feature common across the type I interferonopathy (T1I) spectrum, phenotypic expression can vary between these disorders, the basis of which remains unclear. We collected cerebrospinal fluid (CSF) and serum from patients with the known T1Is Aicardi-Goutières syndrome (AGS) and STING-associated vasculopathy with onset in infancy (SAVI), from individuals with presumed monogenic T1Is (pT1I), from cases of childhood-onset neuropsychiatric systemic lupus erythematosus (nSLE), and from children with non-IFN related autoinflammation (AI) and non-inflammatory hydrocephalus (serving as controls). We measured IFN-alpha protein using digital-ELISA. Eighty-four and 60 measurements were recorded respectively in CSF and serum of 42 patients and 6 controls. In an intergroup comparison of the CSF data (taking one sample per analysed individual), the median level of CSF IFN-alpha was elevated in AGS, SAVI, pT1I and nSLE compared to AI and non-inflammatory controls, with levels highest in AGS compared to all other groups. In AGS, CSF IFN-alpha concentrations were higher than in paired serum samples. In contrast, serum IFN was consistently higher compared to CSF levels in SAVI, pT1I and nSLE. Whilst IFN-alpha is present in the CSF and serum of all IFN-related diseases studied here, our data suggest that the primary sites of IFN production in the monogenic type I interferonopathies AGS and SAVI are, respectively, the central nervous system and the periphery. These results likely reflect tissue specificity in the expression, or biological redundancy, of the mutated gene, and/or in the generation of the endogenous self-nucleic acid ligands presumed to trigger the IFN response observed in AGS.

Poster No. 057

Leigh-like syndrome associated with common LHON mtDNA mutations, m.11778G>A and m.3460G>A

C FRATTER[1], E DOMBI[2], J CARVER[2], K SERGEANT[1], C SMITH[1], MA KURIAN[3], S MORDEKAR[4], C LIANG[5], S BRADY[6], V NESBITT[6], J POULTON[2]

[1]Oxford Genetics Laboratories, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford, UK; [3]Department of Neurology, Great Ormond Street Hospital for Children, London, UK; [4]Department of Paediatric Neurology, Sheffield Children's Hospital, Sheffield, UK; [5]Department of Neurogenetics, Royal North Shore Hospital, Sydney, Australia; [6]NHS Highly Specialised Services for Rare Mitochondrial Disorders, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Objectives: The mitochondrial DNA (mtDNA) variants, m.11778G>A and m.3460G>A, are the two most common variants associated with Leber hereditary optic neuropathy (LHON), accounting for 66% and 14% of LHON respectively. However, in rare cases, these variants have been associated with severe mitochondrial disorders, particularly Leigh syndrome. We report clinical and molecular findings in four such patients, and explore possible causes of their severe symptoms.

Methods and Results: Four unrelated patients with Leigh-like syndrome and no alternative cause for their symptoms were tested via the mitochondrial diagnostic service and found to be homoplasmic for a common LHON mtDNA variant: 3 homoplasmic for m.11778G>A and 1 homoplasmic for m.3460G>A. Muscle was available from one patient and mtDNA copy number analysis indicated borderline mtDNA depletion. This is consistent with a previous report that mtDNA copy number inversely correlates with risk of symptoms in individuals harbouring LHON associated variants. Fibroblasts were available from two patients enabling study of mitophagy, mitochondrial membrane potential and mtDNA copy number by high content fluorescence microscopy. Mitophagic flux was increased, particularly under energetic stress. There was also evidence of low membrane potential and increased mtDNA copy number. This suggests that mitochondrial dysfunction drives mitophagy in these patient fibroblasts, which then leads to increased mitochondrial biogenesis to compensate.

Conclusions: Clinical and molecular findings in four patients with Leigh-like syndrome associated with common LHON mtDNA variants are presented, including evidence of reduced mtDNA copy number in muscle from one patient and increased mitophagic flux in fibroblasts from two patients. We hypothesise that excessive mitophagy may exceed mitochondrial biogenesis in brain tissue of affected patients, hence leading to reduced mtDNA copy number. This could contribute to severe mitochondrial dysfunction in brain which underlies the Leigh-like phenotype.

Poster No. 058

Joubert Syndrome as a model for Whole Genome Sequencing (WGS) analysis

S JAYAWANT[1], M SHANKS[3], M SMITH[4], P CLOUSTON[3], AH NEMETH[2, 5]

[1]University of Cambridge Medical School, Cambridge, UK; [2]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; [3]Oxford Regional Genetics Laboratory, Oxford, UK; [4]Department of Paediatrics, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [5]Oxford Centre for Genomic Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Joubert Syndrome (JBTS) is a genetic neurodevelopmental disorder. Clinical features include cerebellar ataxia as well as systemic abnormalities such as cystic renal disease and hepatic dysfunction. Neuroimaging reveals the "molar tooth sign" (MTS), a characteristic (but not pathognomonic) hindbrain abnormality. Genetic counselling and long-term monitoring of systemic complications requires accurate molecular diagnoses. There are 35 known JBTS genes and most are inherited as autosomal recessive traits, with two mutations expected to be found. Currently, genetic testing for JBTS only analyses coding regions of selected gene "panels". WGS is soon to replace this but, due to its size and complexity, the entire genome will not be analysed, limiting the utility of this technology. To understand how we can improve WGS analysis, we investigated genetic results of 101 likely JBTS cases, referred to the Oxford NHS Molecular Genetics Laboratory. In total, only 45% of cases had a confident molecular diagnosis, based on two mutations being identified in the same gene. In 27% of cases, no mutations were found; these mutations may be present in untested genes, including those associated with non-JBTS syndromes that have the MTS. Most interestingly, in 28% of cases, mutations in

one or more different JBTS genes were identified. This suggests that some mutations may be located in non-coding regions and are being missed. WGS is a potential solution to these "missing mutations", but requires specific Bioinformatic pipelines to be developed. These include: performing analyses on the non-coding regions of a small selection of genes as well as analysing a wider set of genes associated with the MTS. Such an approach may improve efficiency without losing critical data. Our clinical and genetic investigations of JBTS suggest that this condition could be a very useful model for developing WGS in clinical practice. Illustrative examples will be presented.

Poster No. 059
SPTBN4-related neurodevelopmental disorder: a case report

R SMITH[1], G CHOW[1], D THOMAS[2], M SURI[3]
[1]Department of Paediatric Neurology, Queen's Medical Centre, Nottingham, UK; [2]Department of Paediatric Respiratory Medicine, Queen's Medical Centre, Nottingham, UK; [3]Department of Clinical Genetics, Nottingham University Hospitals, Nottingham, UK

Background: The clinical and genetic heterogeneity of neurodevelopmental disorders poses a significant diagnostic challenge, but Whole Exome Sequencing (WES) has become a powerful and valuable tool in the identification of de novo and inherited genetic mutations. Some of these mutations have only been isolated and described within the last few years, with very small numbers of reported cases. Reporting of additional cases is important to add to a limited knowledge base.
Materials and Methods: We report the case of a 3-year old girl, born at term following a normal pregnancy to consanguineous parents who presented with hypotonia and developmental delay in infancy. She initially fed by breast and bottle, but subsequently required a gastrostomy due to recurrent chest infections. Biochemical investigations for metabolic causes as well as neuroimaging were largely normal. Initial genetic testing was negative, including a congenital myasthenia panel as well as molecular diagnostic tests for spinal muscular atrophy, Prader-Willi syndrome and myotonic dystrophy. However, a muscle biopsy demonstrated myopathic features with marked fast fibre predominance. NCS repetitive nerve stimulation was normal. EMG showed chronic partial denervation in the hands and legs bilaterally, suggestive of a motor neuronopathy.
Results: Trio WES identified homozygosity for a pathogenic frameshift variant in the SPTBN4 gene, with parents found to be heterozygous carriers.
Conclusion: SPTBN4-related neurodevelopmental disorder was first reported in June 2018 in five families, and to date, only fourteen cases have been reported in the literature. The SPTBN4 gene encodes the neuronal βIV spectrin subunit. Patients with mutations in this gene present with a severe neurodevelopmental syndrome that includes congenital hypotonia, muscle weakness, areflexia, global developmental delay, feeding and respiratory difficulties and axonal motor neuropathy/neuronopathy. There is evidence of denervation and atrophic muscle fibres on muscle biopsy, and cortical visual impairment and auditory neuropathy associated with hearing loss.

Poster No. 060
SETBP1 gene deletion as a cause of severe expressive language disorder and facial dysmorphism

A OYEGUNLE, J KUTTY
Department of Paediatrics, South West Acute Hospital, Enniskillen, Co Fermanagh, UK

Objectives: Children with isolated speech and language problems and otherwise normal development are often not genetically evaluated, despite recent identification of multiple chromosomal and single gene disorders associated with them. SETBP1 gene deletion on chromosome 18 (mental retardation, autosomal dominant 29 syndrome MRD29) can cause expressive language problems, intellectual disability and distinctive facial features including long face, epicanthic folds, short palpebral features and thin upper lip. The precise function of SETBP1 protein is uncertain, but levels are highest during brain development before birth. Affected persons may have behavioural problems, epilepsy and they often communicate using gestures or by mimicking the expression of others. There have been less than 10 cases reported worldwide.
Methods: A 3 year old male, born to non-consanguineous parents presented with a first febrile convulsion. On examination, he had subtle facial dysmorphic features including hypertelorism, short and downslanting palpebral features, mild periorbital fullness, long and smooth philtrum and thin lips. He had severe expressive language deficit with preserved receptive language skills and some behavioural problems. Hearing assessment was normal including otoacoustic emissions and free field play audiometry. His dysmorphic features prompted genetic investigations.
Results: Array CGH analysis of DNA from the child identified a deletion of approximately 8.438Mb from bands q12.2 to q12.3 in the long arm of chromosome 18. Copy number loss of this region is associated with MRD29 syndrome. He has a 50% risk of passing this deletion to any of his offspring.
Conclusions: In contrast to genetic syndromes, isolated speech and language disorders may be overlooked, as they often present without clearly defined clinical features in a child with normal or mild developmental delay. This case highlights the importance of a precise molecular diagnosis, which in turn could aid the clinician in optimal clinical management, targeted interventions and genetic counselling of family.

Poster No. 061
How often and in which children are biotinidase requests diagnostic?

L WILSON[1], K DEATON[1], C HART[2], S YAP[3], AR HART[1]
[1]Paediatric Neurology, Ryegate Children's Centre, Sheffield Children's NHS Foundation Trust, Sheffield, UK; [2]Department of Clinical Chemistry, Sheffield Children's NHS Foundation Trust, Sheffield, UK; [3]Department of Metabolic Medicine, Sheffield Children's NHS Foundation Trust, Sheffield, UK

Introduction: Biotinidase deficiency is considered in young children with the combination of metabolic acidosis, epilepsy and abnormal skin rashes, or those with early developmental impairment (EDI). The range of phenotypes for biotinidase deficiency is not fully clear in the medical literature.

Objective: To examine the clinical features of children and young people in whom biotinidase testing was requested, and to determine how frequently a positive result was found.
Methods: A retrospective audit of biotinidase requests received by the metabolic laboratory in Sheffield Children's Hospital between 01/01/18 and 30/06/19. All requests were analysed to look at the patient demographics and indication for testing. We determined how often tests were diagnostic and the clinical features of these children.
Results: 823 samples received. 3.5% were ≤1month old, 15.2% >1-month to <1year, 40.9% ≥1 to <4years, 30.9% ≥4 to <10years and 9.5% ≥10 years. 66.2% male and 33.8% female. The reasons for requesting biotinidase were seizures <6months old (3.3%), seizures >6months (17.9%), early developmental impairment (39.5%), autism (4.6%), other (17.1%) and no details (17.6%). 4 (0.48%) results were ≤1.0U/L. 3 were of no clinical significance because another diagnosis was made (such as genetic epilepsy) or repeat testing was normal. Biotinidase deficiency was diagnosed in 1 (0.12%) neonate with severe metabolic acidosis.
Conclusions: The diagnostic yield of biotinidase testing is low, but biotinidase deficiency is a potentially treatable condition. Further research should focus on determining the full spectrum of clinical features of biotinidase deficiency so we know which patients would benefit from testing.

Poster No. 062
Another child with unexplained paroxysmal phenomena

K KALRA, R KNEEN
Alderhey Children's Hospital, Liverpool, UK

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 063
Acute encephalopathy related to cardio-facio-cutaneous syndrome with KRAS mutation

M MONAGHAN[1], F HANNON[1], M LIKEMAN[3], N STOODLEY[3], A DONALDSON[5], D OLLIFE[4], MR CARTER[2], AA MALLICK[1]
[1]Department of Paediatric Neurology, Bristol Royal Hospital for Children, Bristol, UK; [2]Department of Paediatric Neurosurgery, Bristol Royal Hospital for Children, Bristol, UK; [3]Department of Paediatric Neuroradiology, Bristol Royal Hospital for Children, Bristol, UK; [4]Department of Community Paediatrics, Gloucestershire Royal Hospital, Gloucester, UK; [5]Department of Clinical Genetics, Gloucestershire Royal Hospital, Gloucester, UK

Background: Cardio-facio-cutaneous syndrome (CFC) is a rare genetic condition affecting up to 300 people globally. The cardinal features of CFC are congenital cardiac anomalies, distinctive facial appearances and skin changes, however, it is also associated with feeding problems, short stature, macrocephaly, hypotonia, speech delay, learning disability and seizures. CFC has phenotypic overlap with Noonan and Costello Syndrome and these are all considered RASopathies. CFC is associated with variants in genes involved in the RAS/MAPK intracellular signalling pathway and is most frequently caused by mutations in BRAF (approximately 75%), MAP2K1 and MAP2K2 (approximately 25%) and infrequently KRAS (approximately 2%).
Case report: We describe a 7 year old girl with CFC caused by a pathogenic KRAS variant. She has distinctive facial features, pulmonary stenosis and atrial septal defect, multiple pigmented naevi and lymphoedema. She also has Dandy-Walker Syndrome with hydrocephalus, poor feeding and faltering growth requiring gastrostomy feeding. She has right eye amblyopia and right optic nerve atrophy. She is able to speak and walk independently but required additional educational support. She presented with fever without a prodrome and a prolonged focal seizure affecting the left side of her body. She had a marked left-sided hemiplegia. Magnetic resonance imaging showed extensive right hemispheric high T2 intensity, swelling of the grey matter structures, and initial restricted diffusion. Infective, auto-immune, and metabolic causes were excluded. Acute encephalopathy with brain oedema has been previously reported in cases of CFC associated with BRAF mutations, but this is the first report in a patient with CFC due to a KRAS mutation. It is postulated that aberrant ERK signalling may lead to excessive central nervous system cytokine production leading to neurotoxicity and encephalopathy. KRAS is upstream from BRAF and this case suggests that aberrant signalling upstream from BRAF can also lead to acute encephalopathy.

Poster No. 064
A case of early onset dopa responsive dystonia associated with a novel mutation in the PPP2R5D gene.

N SCHINDLER[1], N THALANGE[2], S HEALES[3,4], S POPE[4], R ARORA[1]
[1]Department of Paediatrics, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK; [2]Al Jalila Children's Hospital, Dubai, UAE; [3]Chemical Pathology, Great Ormond Street Hospital NHS Foundation Trust, London, UK; [4]Neurometabolic Unit, National Hospital of Neurology and Neurosurgery, UCLH Foundation Trust, London, UK

Introduction: Dopa responsive dystonias are a heterogeneous group of disorders resulting from disruption of the dopamine synthetic pathway and characterised by primary dystonia which improves following treatment with dopamine. They are rare, yet clinically important because of their good response to treatment. Mutations in the PPP2R5D gene are associated with intellectual disability, hypotonia, epilepsy, and dysmorphism. More recently a specific PPP2R5D mutation has been reported in associated with early onset Parkinsonism in young adults.
Methods: Case notes and literature review.
Results: The patient was first noted to have dystonic episodes at 18 months in the context of global developmental impairment, hydrocephalus, recurrent respiratory infections due to aspiration, and dysmorphic facial features. Movements were episodic, repetitive over several hours, and characterised by rigidity with tremor and limb dyskinesia. Repeated episodes were associated autonomic changes. Episodes only occurred in wakefulness and appeared distressing. Standard and sleep deprived EEG were unremarkable during and between clinical episodes. Whole exome sequencing identified a PPP2R5D mutation chr6:g.42975003G>A. CSF neurotransmitters showed low 5-methyltetrahydrofolate (25 nmol/L, reference range 46-160). MRI brain at 1 year of life was unremarkable with the exception of hydrocephalus, and a repeat at 14

years showed no new changes. Muscle biopsy was able to exclude primary respiratory chain defects. There was some modest initial improvement with a combination of Clonazepam and Folinic Acid. Following CSF neurotransmitter sampling the patient was commenced on Sinemet (Co Careldopa and Levodopa). This resulted in sustained improvement in gait, mood, and clarity of speech.

Conclusion: L-dopa may have a role in non-typical dopa-responsive dystonias. The pathophysiology and clinical applications of this are not yet well understood, and merit further research.

Poster No. 065

Could early treatment with Betaine in patients with infantile forms of MTHFR gene mutations and hyperhomocysteinemia prevent later complications and improve the neurodevelopmental outcome?

M ELGAMAL, TS RAO

Bedfordshire Hospitals NHS Trust, Luton, UK

Background: Methylenetetrahydrofolate reductase (MTHFR) deficiency is an autosomal recessive metabolic disorder of folate metabolism caused by mutations in the MTHFR gene. 5MTHFR deficiency affect Homocysteine remethylation process. This will primarily affect cerebral methylation leading to slow brain growth and poor neurological outcome. Age and severity of clinical presentation will usually correlate with residual enzyme activity. Median age of onset of symptoms is around 1.25 month, according to previous published literature.

Case: Here we present a patient who was born by uncomplicated delivery at term for consanguineous parents. Previous sibling was diagnosed with possible PHACE syndrome and died at 8 months of age where no genetic diagnosis was reached. Index child presented at 1 month of age with microcephaly (OFC 0.4th centile), developmental delay and roving eye movements. Investigations revealed visual loss at the cortical level. MRI brain showed biventricular dilatation, prominent subarachnoid space and some degree of delayed brain myelination. At 1 year of age, the condition was further complicated by the development of cerebral venous thrombosis, intracranial haemorrhage and hydrocephalus followed by onset of infantile spasms. At that time, Homocystiene level was high at 90μmol/l (0–1nmol/ml), with low normal methionine level 17μmol/l (19–51nmol/ml). Genetic test confirmed a homozygous sequence change in MTHFR gene C1408G>T. Since then patient was commenced on long term therapy of betaine and folinic acid. Despite treatment, patient continued to have poor neurodevelopmental outcome and recurrent admissions for respiratory failure.

Conclusion: MTHFR deficiency is a potentially treatable neurometabolic condition. Previous studies have shown that in infantile forms, best outcome is seen in patients who have been treated with Betaine right from birth compared to the untreated group. Therefore, consideration of prenatal diagnosis should be encouraged in high risk groups.

Poster No. 066

Homozygous CSF1R-related disorder with cortical malformations, intracranial calcification and skeletal dysplasia

LMC GREEN[1], J CAMPBELL[2], G VADLAMANI[1]

[1]*Department of Paediatric Neurology, Leeds Teaching Hospitals Trust, Leeds, UK;*
[2]*Department of Clinical Genetics, Leeds Teaching Hospitals Trust, Leeds, UK*

Objectives: Colony stimulating factor 1 receptor (CSF1R) is essential for macrophage development, including microglia and osteoclasts. Mono-allelic CSF1R mutations result in adult-onset leukoencephalopathy with axonal spheroids and pigmented glia which presents from the 4th decade with cognitive and motor decline. More recently 9 cases of bi-allelic CSF1R mutations have been reported with wide-ranging phenotypes including congenital onset with cortical malformations, childhood regression and cognitive and motor decline, each with skeletal abnormalities. Here we describe a 10th case of bi-allelic CSF1R-related disorder, and only the third case with congenital onset.

Case: A male infant was delivered at 37 weeks due to gross congenital ventriculomegaly and shortening of long bones on antenatal scanning. He was the third child of consanguineous Asian parents with previous early miscarriage but no other family history. He had macrocephaly, left sided cataract and right coloboma with an abnormal optic disc and was hypotonic from birth. In the neonatal period he manifested hypocalcaemia, hypophosphataemia and a raised PTH, with an elevated CK >1000. He went on to require ventriculo-peritoneal shunting to manage his hydrocephalus. He later developed seizures; his EEG showed severe slowing with multifocal spikes. He made minimal developmental progress and died aged 9 months after developing respiratory failure requiring prolonged ventilation.

Results: MRI demonstrated significant intracranial malformations including ventriculomegaly, a posterior fossa cyst, fused basal ganglia, hypoplastic cerebellum and multiple areas of periventricular calcification. Skeletal imaging demonstrated global irregularity of long bone metaphases with increased density in keeping with dysplasia and osteopetrosis. Muscle eye brain disease was considered, but felt unlikely due to intracranial calcifications and skeletal

abnormalities. Whole exome sequencing revealed homozygous CSF1R (c.2124T>A) mutation.
Conclusions: This case furthers our understanding of the clinical spectrum of CSF1R-related disorders, in particular the more severe congenital phenotype, and also highlights it as an important differential for patients with intracranial calcification.

Poster No. 067
A case report of biotin thiamine responsive basal ganglia disease

K KALRA, R MADHU
Alder Hey Children's Hospital, Liverpool, UK

Biotin-thiamine-responsive basal ganglia disease (BTRBGD) is a rare treatable neurometabolic autosomal recessive disorder caused by mutation in SLC19A3 gene. Its onset is in childhood characterized by subacute encephalopathy with confusion, dysarthria, convulsions, dystonias and dystonia. This is a progressive condition and can lead to quadriparesis and eventually death if left untreated. The brain MRI usually shows altered signals in basal ganglia, along with grey and white matter abnormalities. We herein present a 2 year old child born to a consanguineous couple, originally from Saudi Arabia. He presented with 2 distinct episodes of neurological symptoms like confusion, unresponsive vacant stares, significant ataxia and weakness with gradual resolution of symptoms within 24 to 48 hours. Neuroimaging showed bilateral symmetrical areas of hyperintensity and diffusion abnormality in the basal ganglia and subcortical white matter. A targeted gene testing showed homozygous mutation in the SLC19A3 gene.

Poster No. 068
Late Onset PPT1-related Batten Disease

T SMITH[1], SA JONES[2], D RAM[1]
[1]Department of Paediatric Neurology, Royal Manchester Children's Hospital, Manchester, UK; [2]Willink Unit, Manchester Centre for Genomic Medicine, Manchester, UK

Introduction: Amongst the varying phenotypes of Batten disease, PPT1-related disease classically presents in infancy. We report a late-onset presentation of PPT1 related Batten disease.
Case: Our patient is an 11 year old girl who first presented at the age of 6 years with learning difficulties and repetitive behaviour. This was initially being investigated locally as Autistic Spectrum Disorder. At the age of 9, she presented with vacant episodes followed by episodes suggestive of myoclonic-absence epilepsy. An EEG showed frequent bursts of spike and wave accompanied by a typical absence seizure. Despite controlling her seizures with antiepileptic drugs, her learning started to deteriorate further. An MR brain showed subtle cerebral and cerebellar atrophy. Urgent neurometabolic investigations demonstrated a very low level of PPT1 enzyme activity. Genetic testing confirmed a compound heterozygous mutation in the PPT1 gene. She presented with visual symptoms at the age of 10 years and currently remains relatively stable from a motor point of view but has gait coordination difficulties. Her epilepsy remains well-controlled.
Discussion: Batten disease describes a group of lysosomal storage disorders which cause neurodegeneration. There are various forms, which may present at different ages with varying outcomes. Traditionally, PPT1-related disease has been associated with an infantile onset between the ages of 6 months and 2 years, with refractory seizures and retinal blindness by the age of 2. Our patient presented much later on with cognitive decline preceding the onset of seizures and eye involvement. PPT1 mutations have only recently been recognised to also present with juvenile onset Batten, expanding the clinical spectrum.
Conclusion: Although there are well-described phenotype-genotype correlations, certain mutations lead to a wide phenotypic range in terms of age of onset and outcomes. Children presenting with cognitive decline even in the absence of seizures and eye involvement warrant testing for Batten disease.

Poster No. 069
Long-term follow-up of a patient with Juvenile Tay-Sachs Disease due to a nonsense (c.78G>A) and a silent (c.1305C>T) variant

A CHRISTOFOROU[1], G ALEXANDROU[2,3], T GEORGIOU[4,5], A DROUSIOTOU[4,5], P NICOLAIDES[2,3]
[1]Imperial College, London, UK; [2]The American Medical Center, Nicosia, Cyprus; [3]University of Nicosia Medical School, Nicosia, Cyprus; [4]The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus; [5]The Cyprus School of Molecular Medicine, Nicosia, Cyprus

Objectives: Tay-Sachs Disease (TSD), also known as GM2 gangliosidosis Type 1, is a rare autosomal recessive neurodegenerative disorder, caused by hexosaminidase A (HexA) deficiency, resulting in excessive accumulation of lipids in neuronal tissue. Presenting features include regression of developmental skills, hypotonia and cognitive decline. Juvenile TSD is very rare, with limited information in the literature. We report the long-term follow up of a 17.5-year-old boy with this form and an unusual genotype: compound heterozygote for a nonsense (c.78G>A) and a silent c.1305C>T variant which has only been reported once before, in a Juvenile Tay-Sachs patient with a mild phenotype.
Methods: Long-term follow-up on a Juvenile TSD case diagnosed at the age of 5 years (2008) and followed up clinically and through serial EEGs and brain MRI.
Results: The patient presented at the age of 4.5 years with language regression, incoordination, gait instability and staring off seizures. Other than mild motor perception difficulties and inattention, his early development was on target, including his speech and language. His plasma Hexosaminidase A was 5% and leukocyte 12%. EEG showed sleep activated right temporal discharges, and his brain MRI was normal. The patient developed gradual loss of motor skills, cognitive decline, spasticity, loss of language, behavioural problems and nocturnal seizures. By 13 years he had lost ambulation, and developed increasing feeding difficulties requiring gastrostomy. Over the past few years however, he has been stable, remains visually alert, able to articulate words, and shows preservation of awareness and cognition and his EEG has normalised.
Conclusion: Juvenile TSD is a very rare neurodegenerative disorder, with patients typically not reaching adulthood. We present

the follow-up of a male with juvenile TSD, over a period of 12 years, showing a milder phenotype with preserved awareness and responsiveness, whose clinical features and seizures have reached a plateau.

Poster No. 070
The effects of enzyme replacement therapy on neuronal ceroid lipofuscinosis type 2 (CLN2) disease: A case report

K NEWARK[1], N SYED[1], F GIBBON[2]
[1]Aneurin Bevan University Health Board, Wales, UK; [2]Cardiff and Vale University Health Board, Cardiff, UK

Objective: Neuronal ceroid lipofuscinoses (NCL) are a group of inherited neurodegenerative disorders that primarily affects children. Genetic testing has led to improved diagnosis and understanding of the molecular mechanisms that underpin these mutations such as the development of targeted therapies. Here, we report a case of the effects of enzyme replacement therapy on a patient with neuronal ceroid lipofuscinosis type 2 (CLN2) disease.
Case report: A female presented aged 3 years with right-sided focal myoclonic seizures. She was born at term, DCDA twin, to non-consanguineous parents, and her father had epilepsy. There was a history of vacant episodes, likely seizures, that occurred from age 12 months. Initial examination revealed normal gross motor development. By aged 4 years, she developed progressive motor and cognitive decline with marked ataxia and speech regression. Her seizures were refractory to treatment despite being on multiple AEDs. Cerliponase alfa, an enzyme replacement therapy of recombinant TPP1, was commenced at aged 5 years via intrathecal route every fortnight. Post treatment, there has been no further seizures, myoclonus has reduced, and her vision has improved. She can now stand independently with a walker and is using more single words.
Results: An EEG done aged 3 years showed several brief bursts of epileptic activity in the posterior regions and synchronous over both hemispheres in keeping with an epileptiform disorder. MRI brain showed enlargement of the cerebellar fissures in keeping with cerebellar atrophy. Genetic analysis identified 2 pathogenic mutations in TPP1 gene indicating CLN2 disease.
Conclusion: With the introduction of cerliponase alfa, the outlook for those with CLN2 disease has improved as it delays disease progression. To have a long-term clinical benefit, treatment must commence early before significant neurodegeneration has occurred. This will require rapid and earlier diagnosis and highlights the importance of developing newborn screening.

Poster No. 071
SCN2A: What else fails?

M TAYLOR, H MCCULLAGH, G VADLAMANI
Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK

Objective: To describe severe gastrointestinal dysmotility in developmental-epileptic encephalopathy due to SCN2A mutation.
Method: A case record review.
Results: A male patient presented at 21 months old with visual impairment, mild dysmorphology, macrocephaly, global hypotonia, hyporeflexia and atonic seizures. Focal seizures, epileptic spasms evolved. He required gastrostomy feeds. Extensive neurometabolic investigations yielded no results but a SCN2A mutation was identified on an epilepsy gene panel. SCN2A: c4551+2T>C whilst absent from the database abolishes the natural donor site from intron 25 and therefore was felt to be pathogenic. His clinical phenotype would be in keeping with a gain of function mutation. At 2 years 8 months, he developed a severe feed intolerance requiring PN (parenteral nutrition). He underwent assessment by the paediatric surgeons and gastroenterologists with no specific cause identified. He remained an inpatient 6 months after admission due to the severe gut dysfunction. His epilepsy was difficult to control with daily seizures up to 3 months prior to the onset of gastrointestinal dysfunction. His seizures were noted to be infrequent as inpatient and vigabatrin was stopped. Topiramate was weaned due to development of renal calculi and the potential for gut adverse effects. So far, he has been seizure free for 7 months continuing a combination of carbamazepine and nitrazepam. He remained on PN, his parents requested for home PN, its appropriateness necessitated multidisciplinary team discussions involving trust ethics committee.
Conclusion: Gut dysfunction is a difficult aspect of SCN2A mutations to manage and this patient presented with a refractory gut failure requiring PN. The severe developmental delay, motor, visual disability and PN dependence constituted an important ethical dilemma in the management. When SCN2A mutation is identified, potential for gut dysfunction should be included in the parental counseling and early gastroenterology involvement should be considered.

Poster No. 072
Clonus with hypotonia: KCNK9 imprinting disorder

M TAYLOR[1], C FORSTER[2], V HARTILL[3], H MCCULLAGH[1]
[1]Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK; [2]Department of Neonatology, Leeds General Infirmary, Leeds, UK; [3]Department of Genetics, Chapel Allerton Hospital, Leeds, UK

Objective: To describe the clinical presentation of a neonate with Birk-Barel intellectual disability dysmorphic syndrome due to KCNK9 Imprinting disorder.
Methods: Retrospective review of patient notes, neurophysiological and genetic data.
Results: A term neonate, who was noted to be small for gestational age on third trimester scan was admitted to neonatal intensive care with hypotonia and aponeas requiring ventilator support on day 2 of life. Clinical examination revealed hypotonia, fixed talipes and clonus, with no dysmorphology. Neuroimaging including MRI Brain and spine were normal. CK was normal at 79. EEG was normal. Genetic testing for trisomies 12, 18, 21, myotonic dystrophy, Prader-Willi syndrome, spinal muscular atrophy and microarray were normal. Extensive neurometabolic investigations yielded no abnormal results. MUSK and anti-acetylcholine antibodies were negative. She was treated for a late onset e. coli sepsis and subsequent galactosaemia testing was negative. A TORCH screen was also completed and was negative. Urgent trio exome sequencing revealed a previously reported heterozygous de novo missense variant, c.706G>A p.(Gly236Arg), in KCNK9 confirming a diagnosis of Birk-Barel intellectual disability dysmorphism syndrome. This is a gene that is normally imprinted with paternal silencing on chromosome 8q24. The disease is caused by a

missense mutation in the maternal copy of KCNK9. In a neonate it is characterised by central hypotonia, joint contractures and clonus. Patients have dysmorphic features, often not apparent at birth including dolichocephaly, a narrow bitemporal diameter, a tented upper lip and medially flared eyebrows which are becoming more in our patient.
Conclusion: The appearance of hypotonia, joint contractures and clonus with normal neuroimaging may act as a prompt to consider a KCNK9 imprinting disorder. It is important to recognise this as there is suggestion from the literature that mefanamic acid may improve clinical outcome by pharmacological enhancement of mutated TASK3 channel current.

Poster No. 073
Recurrent encephalopathy with psychosis and catatonia in a teenage girl due to heterozygous mutation in the CACNA1D gene

M AGABNA[1], R THOMASSON[2], A IYER[1], A JACOB[3], R KNEEN[1]
[1]*Paediatric Neurology, Alder Hey Children NHS Foundation Trust, Liverpool, UK;* [2]*Department of Neurology, Salford Royal NHS Foundation Trust, Salford, UK;* [3]*Department of Neurology, The Walton Centre NHS Foundation Trust, Liverpool, UK*

Case report: A 14 year old girl with learning disabilities and subtle dysmorphic facial features presented sub-acutely with a progressive change in behaviour, parkinsonian features and catatonia. She relapsed three times over 4 years. Each episode lasted several weeks, with a similar clinical course. Brain imaging, infection, endocrine and occult malignancy screens were negative. VGKC-complex autoantibody titres were elevated (711pmol /L): LGI1/CASPR2 were negative. She was treated with immunomodulation: methylprednisolone, intravenous immunoglobulin plasma exchange, rituximab and cyclophosphamide. The treatment appeared to result in a symptomatic improvement; VGKC-complex autoantibody levels normalised. As the features were unusual for VGKC associated encephalitis (no seizures, relapsing course, catatonia) with a background learning difficulties a unifying aetiology was still considered, especially as she relapsed on maintenance immunomodulatory treatment. The karyotype, chromosomal microarray analysis, and a very detailed metabolic screen were normal. She was eventually found to be heterozygous for the CACNA1D c.2305G>A, p.(Ala769Thr) variant through the 100,000 Genomes Project which was considered to be pathogenic.
Discussion: Relapsing encephalopathy is rare. The differential includes autoimmune or paraneoplastic encephalitis, endocrine and metabolic disorders. Genetic disorders are not commonly considered as a cause. This case demonstrates that VGKC antibodies may not be pathogenic and other causes should be considered, especially if the clinical course is unusual. The availability of new genetic technology eventually gave a unifying genetic diagnosis (CACNAD1 gene mutation) that explained all her features. Calcium Voltage-Gated Channel Subunit Alpha1 D (CACNAD1) variant mutation cause gain of function. It is associated with neurological symptoms ranging from learning difficulties, global developmental delay, seizures, movement disorders and neuropsychiatric symptoms. It is also associated with primary aldosteronism; which our patient did not have. There is only one reported case of (A769T) variant, and twelve cases with other CACNAD1 variants. It is important for paediatric neurologists to be aware of the presentation of this CACNAD1 mutation, especially as it can mimic an autoimmune mediated encephalopathy.

Poster No. 074
Paroxysmal dyskinesia due to SCN8A mutation: expanding phenotype.

TO JEJE[1], SR MORDEKAR[1], DS JOHNSON[2], GE GENOMICS ENGLAND RESEARCH CONSORTIUM[3]
[1]*Paediatric Neurology, Sheffield Children's NHS Foundation Trust, Sheffield, UK;* [2]*Sheffield Clinical Genetics Service and EDS National Diagnostic Service, Sheffield, UK;* [3]*The National Genomics Research and Healthcare Knowledgebase v5, Genomics England, UK*

Objective: SCN8A mutations have been described with early onset epileptic encephalopathy and cognitive regression. We report a 4 year old boy with paroxysmal dyskinetic movement disorder with cognitive difficulties who was diagnosed to have SCN8A mutation via whole genome sequencing.
Method: Retrospective case study.
Results: A 4 year old boy born to non-consanguinous parents following an uneventful pregnancy and normal birth presented at 9 months of age fully conscious with intermittent dyskinetic tremulous movements. He had a normal EEG, MRI brain, normal CSF protein, glucose, lactate and neurotransmitters. He was started on Acetazolamide with good response to his movement disorder. Trio whole genome sequencing by the 100000 genome project analysis showed a likely pathogenic variant in SCN8A at c.4832T>A p.(Val 1611Asp). At 4 years of age he has independent mobility, runs with a broad based ataxic gait, intermittent dyskinetic movement disorder, emerging intellectual disability, speech impairment with social communication difficulties but no epilepsy. SCN8A encodes the voltage gated sodium channel Nav 1.6 and is widely expressed in the brain. Functional studies of SCN8A mutations showing gain of function (GoF: 95%) are commonly associated with early onset epileptic encephalopathy responding to sodium channel blockers (SCB) and ketogenic diet. SCN8A mutation functional studies showing loss of function (LoF: 5%) are associated with intellectual disability, autism, dyskinesia often without epilepsy with poor response to SCB. Our child has had a good response to Acetazolamide for his dyskinetic movements which has not been reported in the literature; the intellectual disability with social communication difficulties remains.
Conclusion: There is an expanding phenotypic spectrum of SCN8A mutation. Acetazolamide should be considered for treatment of dyskinetic movement disorders in children with SCN8A mutation without epilepsy.

Poster No. 075
A new clinical phenotype of isolated sulphite oxidase deficiency: A journey to the diagnosis

U KHALID[1], H LEFROY[3], AH NÉMETH[2,3], Z MAUNSELL[1], H ROBINSON[5], S ELLARD[4], R JOSEPH[1], A ROMSAUEROVA[1], RR RATTIHALLI[1]
[1]*Oxford University Hospitals NHS Foundation Trust, Oxford, UK;* [2]*Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK;* [3]*Oxford Centre for Genomic Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK;* [4]*Department of Molecular Genetics, Royal Devon and Exeter NHS*

Foundation Trust, Exeter, UK; [5]Royal Devon and Exeter NHS Foundation Trust, Exeter, UK

Objective: We describe the journey from presentation to diagnosis in a case of Isolated Sulphite Oxidase Deficiency (ISOD) caused by a likely pathogenic homozygous missense mutation in the SUOX gene. We highlight a newly described clinical phenotype, the clinical utility of rapid whole exome sequencing and the importance of a multidisciplinary approach in making rare diagnoses.
Method: Previously fit and well 4 month-old male, only child to non-consanguineous Caucasian parents, presented with a 1 day history of being unsettled. He had paucity of movement on the left. Over the next few days he developed dystonia and seizures, requiring intensive care. He had two MRI brain scans, blood and CSF studies for routine metabolic screens, electroencephalogram, muscle biopsy and trio whole exome sequencing. He stayed in hospital for 8 days and was transferred to a hospice for symptomatic management, where he died 6 weeks after his initial presentation.
Results: MRI Brain on the day of presentation showed large wedge-shaped area of restricted diffusion involving the right frontal, lateral temporal and anterior parietal lobe with areas of restricted diffusion in the right and to lesser extent left basal ganglia. On day 6 imaging demonstrated significant deterioration with extensive signal change involving both cerebral hemispheres and basal ganglia. Trio exome sequencing identified a biparentally inherited homozygous missense variant in the SUOX gene (c.734T>C p.(Leu245Pro)), initially classified as a Variant of Unknown Significance (VUS). Subsequent specialist metabolic investigations revealed a raised urine sulphocysteine level, enabling the VUS to be reclassified as likely pathogenic, in keeping with a diagnosis of ISOD.
Conclusions: A multidisciplinary approach led to rapid whole exome sequencing, enabling a newly described phenotype of this disorder to be identified. The correct classification of the genetic variant and a secure diagnosis provides the parents with accurate information and reproductive options for future pregnancies.

Poster No. 076
The diagnostic conundrum: MRI mimicking mitochondrial disorder in SCN8A EIEE

M TAYLOR, S ALI, G VADLAMANI, H MCCULLAGH
Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK

Objective: To describe clinical and radiological phenotype of a case of SCN8A encephalopathy mimicking a mitochondrial disorder.
Method: Review of clinical records and MR imaging.
Results: A male child born after an uneventful pregnancy and delivery at term presented with neonatal seizures on day 1 of life. Initial neuroimaging, neurometabolic investigations and microarray results did not provide a specific diagnosis. At 3 months, he was profoundly hypotonic with lack of visual maturation. At 5 months, no developmental progress had been made and an evolving peripheral dyskinesia was evident. An MRI brain was repeated which showed high signal in both optic radiations; in the midbrain centered on the red nucleus; in the tectum; the dorsal brain stem at the pontine level and at the lower end of the medullary olives. This led to investigations for a mitochondrial disorder that were negative. His developmental delay was severe, he was profoundly disabled with a pharmaco-resistant epilepsy. An MRI brain at 6 years of age showed improvement in the areas of previous abnormal T2 signal, but demonstrated symmetrical cerebral cortical and cerebellar atrophy with thinning of the corpus callosum. An early onset epileptic encephalopathy gene panel yielded a de novo mutation in SCN8A (p.Arg850Gln). Whilst the phenotype is suggestive of a gain-of-function mutation it has not been subjected to functional analysis. Arg850 is known to be a positively charged amino acid and the change to glutamine is felt to affect the activation of voltage-gated sodium channels subunit Nav1.6.
Conclusion: Optic radiation involvement and cerebral atrophy on MRI mimicking a neurodegenerative disease has been described in the literature for children with SCN8A mutations. Our case illustrates clinical and MR findings mimicking a mitochondrial disorder in SCN8A EIEE, however identifying the early optic radiation involvement may act as a prompt to consider EIEE gene panel.

Poster No. 077
A case of Jacobsen syndrome with acetazolamide responsive ataxia and non-progressive leukodystrophy.

CB GAVIN[2], R ARORA[1], O TAYO[1]
[1]Jenny Lind Children's Hospital, Norfolk and Norwich University Hospital, Norwich, UK; [2]Norwich Medical School, University of East Anglia, Norwich, UK

Introduction: Jacobsen syndrome is a rare contiguous gene syndrome caused by partial deletion of the long arm of chromosome 11 with around 200 cases reported worldwide. Patients with typical features of Jacobsen syndrome show intellectual disability, short stature, congenital heart defects, thrombocytopenia, and characteristic facial features. White matter abnormalities in Jacobsen syndrome are not well described – a recent case report study suggests that WMA in JS are due to chronic white matter edema associated with HEPACAM/Glial/CAM deletion and show gradual improvement over time, as seen in some MLC2B patients.
Methods: Case notes and literature review.
Results: A 7-year-old boy with Jacobsen syndrome was born weighing 2.65kgs to genotypically normal, non-consanguineous parents. There were concerns IUGR, feeding difficulties and facial and limb dysmorphism. At 1 month his head circumference was in the 25th centile, changing to the 91st centile at 1 year 10 months; his gait was delayed, broad based and ataxic. At 2 years of age, an MRI showed bilateral periventricular T2 hyperintensities within the deep white matter in the parietal and frontal lobes with sparing of subcortical white matter. At 4 years of age, due to progressive ataxia, he was commenced on acetazolamide. Within 3 months, a dramatic improvement in ataxia was seen with the ability to run and walk independently and climb steps with a further improvement in fine motor skills. A repeat MRI scan at 7 years old showed improvement in leukodystrophy which was in keeping with his recent neurological examinations and improvements in ataxia and global development.
Conclusions: We present an interesting case of a Jacobsen syndrome with acetazolamide responsive ataxia and non-progressive leukodystrophy. With the lack of current literature linking ataxia and Jacobsen syndrome, this case study highlights the need for more research to explore if acetazolamide may accelerate clinical improvement before radiological improvement.

Poster No. 078

A de novo missense variant in PPP2R5D in a 15 month old patient with hypotonia, macrocephaly and developmental delay

A SYED, A MAJUMDAR
Department of Paediatric Neurology, Bristol Children's Hospital, University Hospital NHS Foundation Trust, Bristol, UK

Objective: To describe case of PPP2R5D-related neurodevelopmental disorder in a 15 month-old caucasian male with macrocephaly-megalencephaly, hypotonia and developmental delay.
Methods and Results: PPP2R5D is a member of the PP2A (serine-threonine-protein phosphatase-2) family with critical role in development including neurodevelopment. PP2A complex is composed of 3 subunits – scaffolding subunit A, regulatory subunit B and catalytic domain C. PPP2R5D encodes the 602-amino acid protein $B56^{\delta}$ - an isoform of subunit B. It is highly expressed in the brain and thought to be involved in cell growth, chromatin remodelling and transcriptional regulation. This holoenzyme interacts with PI3/AKT growth regulatory cascade. Our patient presented in the second month of life with faltering growth and macrocephaly (OFC>99th centile). He had significantly reduced tone with normal reflexes. His cranial imaging (CT/MRI/ultrasound) showed macrocephaly with megalencephaly with no evidence of raised intracranial pressure. At 12 months of age he was unable to hold his head up independently for prolonged periods of time. He could sit with support in an orthotic suit, fix and follow with eyes, smile responsively. He had ongoing low tone with antigravity movements in all limbs and good hand function.
Conclusions: On Exome Trio sequencing, a de novo heterozygous missense variant c.592G>A(Chr6:g.42975003G>A) was detected. This is predicted to cause protein change (p.Glu198Lys) - this would result in altering a highly conserved negatively charge glutamic acid to a positively charged lysine thereby affecting protein structure. It disrupts PP2A subunit binding and impairs dephosphorylation of specific substrates. Analysis of his unaffected parents showed no evidence of variant. PPP2R5D pathogenic variants are an important cause of neurodevelopmental delay associated in macrocephaly, hypotonia, epilepsy and autism and are not currently identified by multigene panel testing. Identification using exome sequencing allows appropriate surveillance for that child and prevents further unnecessary invasive investigations such as muscle biopsy.

Poster No. 079

A rare case of vanishing white matter leukodystrophy

N CONQUEST[1], M CHITRE[2], SG MEHTA[3], L RAYMOND[3], B MUKHTYAR[1]
[1]Department of Paediatrics/Paediatric Neurology, Norfolk and Norwich University Hospital, Norwich, UK; [2]Department of Paediatric Neurology, Addenbrooke's Hospital, Cambridge, UK; [3]Department of Clinical Genetics, Addenbrooke's Hospital, Cambridge, UK

Case summary: A 5 year old boy was referred to clinic with leg pains and progressively unsteady gait over several months. There was a history of clumsiness/ frequent falls since age 2. He also had hand 'shakes'- more evident during activities. There was a clear history of deterioration of symptoms at time of illness. During febrile illnesses, he would become more unsteady, tremors would worsen, and speech became unclear. He would have word finding difficulties and difficulties in initiating sentences following an illness. This would take up to 6 weeks to improve and return to baseline. Developmentally, he walked before age one, but walked on tiptoes. He was able to climb, run, but not as well as his peers. Fine motor skills were delayed. He was toilet trained by age 2, but during the illnesses he would have accidents. Speech was delayed. He had recurrent glue ear and conductive hearing loss. On examination, he walked on tiptoes, gait was unsteady. Lower limb tone was increased, reflexes were brisk, ankle clonus present bilaterally. Planters were upgoing. He was able to stand on each foot for 3 seconds. He had an intention tremor on finger nose testing. There was no nystagmus or dysdiadokokinesia. MRI brain - diffusely abnormal white matter signal in T2 with evidence of poor myelination. He was recruited in the Next Generation Children Study. Whole genome sequencing revealed Pathogenic compound heterozygous variants detected in the EIF2B2 gene – consistent with diagnosis of autosomal recessive leukoencephalopathy with vanishing white matter disease.
Discussion: Vanishing white matter leukodystrophy is characterized by variable neurologic features including progressive cerebellar ataxia, spasticity, and cognitive impairment associated with white matter lesions on brain imaging. We describe genetics, radiological, and clinical features including prognosis of this rare condition.

Poster No. 080

Soto's syndrome presenting as recurrent neonatal and infantile sleep apnoeas

G KURUVILLA[1], R ARMSTRONG[2], L RAYMOND[2], T POLYCHRONAKIS[3], A PILLAI[3], B MUKHTYAR[4]
[1]Department of Paediatrics, Norfolk and Norwich University Hospital, Norwich, UK; [2]Department of Clinical Genetics, Addenbrooke's Hospital, Cambridge, UK; [3]Department of Paediatrics/Respiratory Paediatrics, Norfolk and Norwich University Hospital, Norwich, UK; [4]Department of Paediatrics/Paediatric Neurology, Norfolk and Norwich University Hospital, Norwich, UK

Case summary: A term male infant was admitted aged 9 days with recurrent apnoeas. He underwent a septic screen and was treated for presumed sepsis. He required high flow nasal cannula oxygen. Cultures were negative, he weaned off oxygen and was discharged home aged day 15. He was readmitted at 23 days age with recurrent apnoeas. On arrival, he was apnoeic and grey. He was commenced on CPAP ventilation. He was hypotonic with distinct features: narrow palpebral fissures, hypertelorism, dolicocephalic skull, umbilical and inguinal hernia. Growth parameters were age appropriate on 25th centile. Peripheral tone, reflexes, spine were normal. Over the next few weeks he underwent several investigations and ENT, Respiratory, Neurology, Genetic reviews. The sleep study was abnormal with clusters of desaturations in periods of active sleep. Further detailed sleep analysis at a tertiary centre confirmed severe sleep disordered breathing, mainly central, with a degree of obstructive sleep apnoea. A direct microlaryngoscopy did not show any clear substrate of obstruction. EEG, MRI brain/spine, EMG, Nerve conduction, microarray and genetic testing for congenital central hypoventilation syndrome did not show any abnormality. He was recruited into the Next Generation Children study (NGC), which identified a de novo pathogenic variant in in the NSD1gene, consistent with Soto's syndrome.

Discussion: Soto's syndrome is an autosomal dominant disorder characterised by pre and postnatal overgrowth, advanced bone age, acromegaly, hypotonia, intellectual disability, occasional brain anomalies and seizures. Otolaryngologic problems like deafness, laryngomalacia, obstructive sleep apnoea have been previously reported. In the absence of other ENT abnormalities in our case, the sleep disordered breathing is thought to be related to central hypotonia in addition to dysmature/abnormal central control of breathing.

Poster No. 081

Pathogenic variant in EARS2 gene consistent with a molecular diagnosis of combined oxidative phosphorylation deficiency 12

CM STEPHENS[1], N MCSWEENEY[1], M MOORE[2], F MOLONEY[2], E CRUSHELL[3]

[1]Paediatric Neurology Department, Cork University Hospital, Cork, Ireland; [2]Radiology Department, Cork University Hospital, Cork, Ireland; [3]Metabolic Department, Temple Street Hospital, Dublin, Ireland

Introduction: We describe a novel case that was compound heterozygous for a c.322C >Tp.(Arg108Trp) and c.328G >Ap.(Gly110Ser), likely pathogenic variants in the EARS2 gene consistent with combined oxidative phosphorylation deficiency 12 presenting in infancy with developmental regression and irritability and later generalised epilepsy.
Methods: Extended mitochondrial DNA testing identified a de novo EARS2 mutation in our proband.
Results: We describe the fourth child of nonconsanguineous parents who presented at 7 months with developmental regression and irritability. Examination revealed persistent primitive reflexes and a spastic paraparesis. Laboratory findings included hyperlactataemia 6.97mmol/L (0.5–2.2) and elevated alanine. MRI brain revealed widespread global symmetrical changes throughout the white matter, basal ganglia and brainstem, consistent with a possible leukodystrophy or toxic leukoencephalopathy. Interestingly, Lysosomal enzymes were normal with no evidence of metachromatic leukodystrophy or Krabbe's. Microarray identified a gain in the short arm of chromosome one. Extended mitochondrial DNA testing identified a de novo EARS2 mutation (compound heterozygous for a c.322C >Tp.(Arg108Trp) and c.328G >Ap.(Gly110Ser), likely pathogenic variants in the EARS2 gene consistent with combined oxidative phosphorylation deficiency 12. At 18 months, she has generalised epilepsy, controlled with Keppra and Frisium, persistent developmental delay, though irritability is ameliorated with Gabapentin.
Conclusions: The EARS2 Gene is located on chromosome 16p12.2 and is key to mitochondrial function. It encodes a member of the class1 family of aminoacyl-tRNA synthetases (glutamyl-tRNA synthetase), which plays an integral part in protein synthesis. Mutations are associated with Leigh-Syndrome and combined oxidative phosphorylation deficiency12 (COXPD12), with up to twenty-three mutations described to date in the latter. COXPD12 is characterized by early-onset hypotonia, developmental delay or regression, hyperlactataemia and hallmark MRI findings of T2-weighted hyperintensities in deep cerebral and cerebellar white matter and brainstem. Prognosis depends on clinical phenotype; mild or severe with some recovery of skills in toddler years in the former.

Poster No. 082

Spastic ataxia with peripheral neuropathy in children due to SACS gene mutation - Autosomal recessive spastic ataxia of Charlevoix-Saguenay, autosomal recessive spastic ataxia type 6

GOWDA[1], D JOSIFOVA[3], T HEDDERLY[1], V CAMPBELL[4], M FERNANDEZ[1], K PAPAGIANNI[1], J O'SULLIVAN[1], A SIDDIQUI[2]

[1]Paediatric Neurosciences, Evelina London Children's Hospital, London, UK; [2]Paedaitric Neuroradiology, Evelina London Children's Hospital, London, UK; [3]Genetics Department, Guy's Hospital, London, UK; [4]Royal Alexandra Children's Hospital, Brighton, UK

Objective: To describe two cases of ARSACS, a neurodegenerative condition caused by mutations in SACS gene, manifested by early onset cerebellar ataxia, lower limb spasticity and peripheral neuropathy.
Method: Case notes review.
Results: Both patients had: (1) unsteady gait, frequent falls noted after starting independent walking (2) specific learning difficulties. Patient-1 (boy) had global developmental delay, autism. Aged 5-years, he manifested high stepping wide-based gait, brisk deep-tendon-reflexes with TA tightness. NCS showed demyelinating peripheral neuropathy. Neuroimaging-1: Mild focal prominence of cerebellar fissures in superior vermis. Neuroimagint-2: Mild progression of previous vermis cerebellar atrophy, mild thinning of upper cervical-cord, abnormal signal within pons (stripy tigroid pattern) and along corticospinal tract. Cardiology, Ophthalmology normal. Genetics: Compound heterozygous mutations in SACS gene - c.826C>T(p.Arg276Cys) and c.1693del(p.Ile565fs) (new). Patient-2 (girl) had longstanding coordination problems, intention tremor, cerebellar gait, foot drop, slow-relaxing-reflexes, dysdiadokenesia. NCS showed demyelinating peripheral neuropathy. Neuroimaging-1: some possible atrophy of the superior cerebellar vermis, some thinning of the cerebellar folia. Neuroimaging-2: Increased signal change in middle and lateral pons, extending along middle cerebral peduncles. Volume of pons relatively preserved. Mild cruciate hyperintensity noted centrally within medulla and cerebral peduncles bilaterally. Genetics confirmed mutation in SACS gene.
Conclusion: ARSACS is seen in all ethnicities and parts of the world. Presentation with spastic ataxias with peripheral neuropathy should prompt consideration of ARSACS, particularly if there is a suggestion of peripheral neuropathy. Neuroimaging could be a helpful pointer.

Poster No. 083

Congenital insensitivity to pain (CIP): A rare disorder with management challenges

S ANIL[1], CG WOODS[2,3], APJ PARKER[1,4]

[1]School of Clinical Medicine, University of Cambridge, Cambridge, UK; [2]Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK; [3]Medical Genetics, Addenbrooke's Hospital, Cambridge, UK; [4]Paediatric Neurology, Addenbrooke's Hospital, Cambridge, UK

Background: Congenital Insensitivity to Pain (CIP) is a very rare genetic disorder with only 2 to 4 new cases per year within the UK. It is characterized by an inability to perceive pain present from birth due to lack of, or malfunction of, nociceptors. Our

aim was to investigate the presentation of CIP and whether it is at risk of mismanagement.
Methods: A retrospective analysis of patients with CIP from across the UK seen in the Paediatric Neurology Department of Addenbrooke's Hospital, Cambridge between 2015 and 2020 was undertaken to identify the presentation of CIP, the incidence of delayed diagnosis, and the prevalence of appropriate surveillance (including ophthalmologic and orthopaedic).
Results: We found a delayed presentation in 5 out of 7, with a low rate of appropriate surveillance. All 7 patients presented with evidence of self-sustained injuries as a result of pain insensitivity, some with severe disease pathologies, such as Charcot joints.
Conclusion: We propose improvement in the approach to managing patients with CIP. Firstly, timely diagnosis leading to earlier intervention and avoidance of confusion with child abuse. A multidisciplinary approach is essential. We recommend at least annual expert orthopaedic and ophthalmologic assessment. This insight into CIP and its potential mismanagement provides a baseline upon which a surveillance study can be carried out to further develop management recommendations.

Poster No. 084
A case of cerebral palsy?

SS CHOWDHURY[1], A PARIDA[1], S CHANDRATRE[1], S JAYAWANT[1], K MAHAL[1],
U KINI[1], R CHINTHAPALLI[2], J GADIAN[1]
[1]Oxford Children's Hospital, Oxford, UK; [2]Great Western Hospital, Swindon, UK

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 085
TSC1 c2640delG mutations are associated with lesions in the head of the caudate

Y COOPER[1], J CROSS[2], APJ PARKER[1, 3]
[1]Clinical Medical School, University of Cambridge, Cambridge, UK; [2]Department of Neuroradiology, Addenbrooke's Hospital, Cambridge, UK; [3]Department of Paediatric Neurology, Addenbrooke's Hospital, Cambridge, UK

Objective: To describe the presentation and surveillance of a neuroradiological abnormality that co-segregates with the TSC1 c2640delG variant in Tuberous Sclerosis Complex (TSC).
Methods: Notes and MRI appearances of all children attending our regional paediatric TSC clinic, covering 4.6 million people, were reviewed. All children with subependymal nodules (SEN) greater than 6mm maximum dimension were identified. Further subclassification included those with SEN involving parts of the caudate remote to the caudothalamic groove (CTG). The CTG is where the subependymal giant cell astrocytomas seen in TSC are typically identified.
Results: Two brothers with the TSC1 c2460delG variant had lesions involving the caudate heads. One was on the right side; one was on the left side. The right caudate SEN was initially inapparent on the first scan aged 2 years. 6 years later it measured 8.3x7.3mm and 2 years subsequently was 8.3x5.9mm. The left caudate SEN was 7.2x3.9mm on the first scan at 15 months of age, and 7.5x3.5mm 10 years later.
Conclusions: Lesions within the caudate head were rare in our cohort of children attending a specialised TSC clinic covering a large population. Only children carrying the same TSC1 variant had these lesions, although on opposite sides. Head of the caudate lesions are likely to be associated with this TSC1 variant. They are unlikely to undergo malignant change over a long period.

Poster No. 086
Watch them walk: abnormal gait – an early clue of CNS disorders

P JENKINS[1], RK SINGH[1], G WILLIAMSON[1], Y SINGH[2]
[1]Department of Paediatrics, Mid Yorkshire Hospitals NHS Trust, Wakefield, UK; [2]Oncology, Barts Health NHS Trust, London, UK

The leukodystrophies are a group of rare disorders which cause white matter abnormalities and demyelination of the CNS. The onset of often non-specific symptoms may be insidious and so patients may go undiagnosed for many years. We present two recent cases whose initial presentations were gait related. There are over fifty known causes of leukodystrophy and more are being discovered every year. Diagnosis is predominantly by MRI and white cell enzymes, with an increasing role for genetic testing. Children can present at different ages depending on the underlying pathology but commonly exhibit progressive loss of function affecting motor, gait, balance, tone, vision, hearing and behaviour in addition to developmental regression. K, aged six, initially presented in September 2017 with tiptoe walking (as shown in the video) and calf pain but no obvious musculoskeletal cause. He re-presented in April 2018 with developmental regression and behavioural changes. An MRI showed diffuse white matter demyelination in keeping with metachromatic leukodystrophy confirmed by genetic analysis. Sadly, he has deteriorated quickly and is now wheel-chair dependent with significant spasticity. E, aged three, initially presented in June 2020 and was diagnosed with irritable hip. With no improvement after 4 weeks he re-presented with an unsteady gait and increased falls. This video shows circumduction gait with an extensor posture of his right leg, pes planus with knock knee and occasional waddling gait, associated with upper motor neuron signs. He had an MRI in July 2020 which showed minor frontal predilection and some subcortical sparing with periventricular cavitation. He is currently awaiting genetic analysis. Therapies for leukodystrophy are most beneficial in the early disease course and early diagnosis is important for establishing supportive care for the patient and their families. Clinical signs such as gait abnormalities can aid early diagnosis and intervention.

Poster No. 087
Identification of individuals with likely AADC deficiency based on DDC variation in the Genomics England (GEL) 100k Genomes Project dataset

L SCHLUETER[1], E FOX[1], V MEHTA[4], R MADHU[3], L MOUTSIANAS[2], C ODHAM[2], C SMITH[2], M RANCE[1]
[1]PTC Therapeutics, Frankfurt am Main, Germany; [2]Genomics England, London, UK; [3]Department of Neurosciences, Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [4]Paediatrics, Hull Royal Infirmary, Hull University Teaching Hospitals NHS Trust, Hull, UK

Objective: Aromatic l-amino acid decarboxylase deficiency (AADCd) is caused by mutations in the DDC gene, which leads to a reduced AADC enzyme activity and a decreased production

of dopamine and serotonin. The aim of this study was to determine the prevalence of AADCd within the GEL dataset.
Methods: Individuals with probable AADCd were based on variations in the DDC gene. Genetic variations, previously described as pathogenic, were considered high confidence. Other rare, potentially damaging, genetic variants were considered low confidence. Further, the data was not phased and genetic variations could not be assigned to a specific allele. Therefore, homozygote individuals were considered high confidence, whereas potentially compound heterozygote individuals were considered low confidence. To prevent reidentification, numbers of 1 to 4 were reported as <5. HPO terms and ICD-10 codes as descriptions for phenotype were used to further evaluate the likelihood of AADCd in these individuals.
Results: We identified <5 homozygote individuals for the variant c.749C>T. They were enrolled in the project for early onset dystonia, which is consistent with AADCd. 12 homozygote individuals were identified for the variant c.629C>T, which has been reported in only one compound heterozygote AADCd patient previously. After evaluating HPO terms and ICD-10 codes, this variant was rated as benign. Less than 5 individuals were identified for potentially compound heterozygote low confidence variants. Intellectual disability, which is a clinical feature of AADCd, is listed as a reason for enrollment in the project for this group. Further diagnostic workup will be required in this group.
Conclusions: Screening for pathogenic variants in the Genomics England dataset, with subsequent phenotypic confirmation is a potentially useful tool to identify patients with rare disease.

Poster No. 088
Delays in diagnosis are associated with poor clinical outcomes in patients with Arginase 1 deficiency

GA DIAZ[1], N LONGO[2], S BATZIOS[3], G BUBB[5], M BECHTER[5], JL MERRITT II[4]
[1]Icahn School of Medicine at Mt. Sinai, New York City, NY, USA; [2]University of Utah, Salt Lake City, UT, USA; [3]Great Ormond Street Hospital NHS Trust, London, UK; [4]University of Washington, Seattle, WA, USA; [5]Aeglea BioTherapeutics, Austin, TX, USA

Introduction: Arginase 1 Deficiency (ARG1-D) is an inherited metabolic disease with elevated plasma arginine and prominent neurological manifestations (spasticity, seizures, and intellectual disability). Although diagnostic testing by plasma arginine is widely available, the variable presentation and rarity of the condition may lead to delayed or misdiagnosis. Given the known impact of plasma arginine reduction with diet and recent advances in the ability to reduce plasma arginine, prompt diagnosis is important in optimizing patient outcomes. The aim of this study was to review the clinical presentation of patients with ARG1-D, including the magnitude of delay in diagnosis.
Method: An extensive review of published English-language literature identified 140 unique ARG1-D cases from 1965 to 2018.
Results: Lower limb spasticity was present in 84% of 117 patients. Intellectual disability was noted in 82% of 97 patients with available data and was moderate or severe in 39% of them. Seizures and upper limb spasticity were present in 70% and 50% of patients respectively and 56% had failure to thrive. Maximal plasma arginine exceeded 4.5x ULN (n=112, ULN=115μM) in >50% of patients. Despite disease management, arginine values remained elevated beyond 200 μM in most patients (n=33). Median age at presentation was 2 years (n=81). Delays in diagnosis by $\geq$2 years were reported in 39% of patients and by $\geq$5 years in 24% of patients; the median age at death was 17 (n=20).
Conclusions: ARG1-D presents with prominent neurological manifestations with significant delays in time to diagnosis. Patients are at risk of progression to develop more severe complications with early mortality. Plasma amino acid analysis to assess arginine levels in patients presenting with spasticity, seizures and cognitive impairment could lead to early diagnosis and earlier initiation of interventions that reduce morbidity and mortality risk in this patient population.

Poster No. 089
A rare cause of new onset refractory status epilepticus (NORSE)

KB BELKHATIR[1], J WEITZ[2]
[1]Paediatrics, John Radcliffe Hospital, Oxford, UK, [2]Paediatric Intensive Care, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

NORSE is a rare but devastating neurologic emergency characterised by the new onset of refractory status epilepticus without a clear acute or active structural, toxic, or metabolic cause, in the absence of a history of epilepsy or other relevant neurological disorder. NORSE occurs more frequently in previously healthy young adults and school-aged children. There is a male predominance in the paediatric population. We present a previously healthy 6-year-old boy, who developed sudden onset flaccid paraparesis followed by progressively worsening myoclonic movements of both upper and lower limbs. An urgent CT and MRI Head and spine were reported as normal. He was initially diagnosed with functional neurological symptoms secondary to anxiety as there was no change in consciousness or observations during these movements. On day 3 of admission, he developed generalised myoclonic movements refractory to APLS medical management. He was therefore intubated following a thiopentone induction and admitted to Paediatric Critical Care. He remained intubated for 3 weeks and required thiopentone, midazolam and fentanyl infusions, in addition to plasmapheresis, immunoglobulins and pulsed methylprednisolone to control RSE. EEG demonstrated myoclonic status epilepticus. Genetics/muscle biopsy identified the underlying cause of the seizures to be a mitochondrial disease secondary to DMN1L mutation. A second MRI head demonstrated basal ganglia, thalamic, hippocampal changes. The patient was established on oral clobazam, phenobarbitone, levetiracetam and ketogenic diet before extubation. He remains on non-invasive ventilation at night. His seizures are well-controlled, and his neuromuscular function continues to improve on the neurorehabilitation ward.
Conclusion: This case illustrates the importance of a prompt work-up of new onset refractory seizures in children. An initial normal MRI head/spine does not preclude a severe condition, like NORSE. Metabolic disorders could present at any age and should be suspected in children presenting with NORSE.

Poster No. 090

Chromosome 1p31 deletion – an indistinct phenotype

K KALRA, AV ISRANI
Alder Hey Children's Hospital, Liverpool, UK

A 14 year old boy was referred for evaluation of abnormal movements, severe learning difficulties and autism spectrum disorder. There was strong family history of ASD and learning difficulties in siblings. Past history is remarkable for orchidopexy and hypospadias's surgical correction. His examination revealed craniofacial dysmorphism with unequal pinna, coarse facial features, wide nostrils and wide mouth consistent with generalized hypotonia with normal deep tendon reflexes, bilateral multiple joint contractures and bilateral cavus deformity of feet. Blood Investigations showed low IgG, IgM, IgA and IgE levels with low antibodies against pneumococcus. Brain MRI showed prominent perivascular spaces and non-specific T2 hyper intensity in periventricular deep white matter. In view of relevant family history and distinct facial features, genetic etiology was considered. His chromosomal microarray confirmed the deletion at chromosome 1p31.1.p31.3.

Discussion: It is extremely rare to find interstitial deletions in short arm of chromosome 1. To best of our knowledge 20 cases with deletions of varying size of 1p31.1p31.3 have been reported so far. Phenotypical characteristics usually include developmental delay, seizures, round face with a prominent nose, micro/retrognathia, half-opened mouth, short neck, hand/foot malformations, hernia, congenital heart malformations, and abnormal external genitalia. and autism spectrum disorder. Neuropsychiatric or behavioral phenotypes for chromosome 1p31 deletion have been poorly characterized to date beyond autism spectrum disorder and intellectual disability. When someone has a large chromosomal anomaly encompassing multiple genes we expect to see problems with development and learning, growth, possible structural anomalies and often a distinctive facial appearance. It is useful to be aware of this condition which presents with non-specific features, and highlights the importance of simple diagnostic tools like chromosomal microarray as part of initial work up of intellectual disability/learning difficulties.

Poster No. 091

Transforming diagnostic confidence in neurodevelopmental disorders using CRISPR-based saturation genome editing

EJ RADFORD[1,2], HK TAN[1], H IRONFIELD[1], M ANDERSSON[1], J STEPHENSON[1,3], S GERETY[1], ME HURLES[1]
[1]Wellcome Sanger Institute, Cambridge, UK; [2]Department of Paediatrics, University of Cambridge, Cambridge, UK; [3]EMBL-EBI, Wellcome Genome Campus, Hinxton, UK

Genetic sequencing is a powerful diagnostic tool in paediatric neurology. However, correctly interpreting candidate genetic variants remains a major challenge. In children, this is compounded by an evolving clinical phenotype, making genotype-phenotype correlation difficult. However, early diagnosis and accurate prognostication is important to families, and may facilitate treatments which reduce future disability. Diagnosis is therefore often attempted before a phenotype has fully evolved. Conventional strategies to resolve variants of uncertain significance rely on the accumulation of clinical data and variant effect prediction algorithms. Clinical data often accumulate too slowly to be useful to families with rare neurodevelopmental disorders. Variant effect prediction algorithms are confounded by circularity and error propagation and are often discordant. New approaches are urgently needed. Saturation genome editing (SGE) utilises CRISPR-Cas9 technologies to specifically engineer thousands of genetic variants into the endogenous genetic locus of a pool of cells and directly test their functional impact in vitro (Findlay et al, 2018). The use of a haploid human cell line (HAP1) simplifies the design and interpretation of genetic screens. As proof-of-principle we have applied SGE to DDX3X, an X-linked RNA helicase of the DEAD-box protein family which is essential in HAP1. Heterozygous DDX3X loss-of-function mutations cause intellectual disability, often associated with hypotonia, movement disorders and/or epilepsy. We have functionally characterised thousands of DDX3X single nucleotide variants, the majority of which have not previously been observed in the human population. Our data show strong concordance with clinically annotated variants and suggest new disease mechanisms. For greatest clinical impact, this approach will need to be scaled across many neurodevelopmental disorders, as these conditions are individually rare. We have identified 157 neurodevelopmental genes accessible to our assay. Such direct functional characterisation of genetic variation at scale has the potential to transform clinical diagnosis.

Poster No. 092

Case report; Hyperekplexia masquerading as an early onset epileptic encephalopathy

A PARIDA[1,3], R KUMAR[1], J MORTON[2], S SERI[4]
[1]Department of Paediatric Neurology, Birmingham Children's Hospital, Birmingham, UK; [2]Department of Clinical Genetics, Birmingham Women's Hospital, Birmingham, UK; [3]Department of Paediatric Neurology, Oxford Children's Hospital, Oxford, UK; [4]Department of Paediatric Neurophysiology, Birmingham Children's Hospital, Birmingham, UK

Introduction: We describe a case report of a term neonate presenting with seizures thought initially to have an epileptic encephalopathy based on electroencephalography (EEG).

Method: Case report.

Results: A baby of first cousin related parents born at term presented with stereotyped events characterised by tonic extension of both arms. It was noted that typical episodes were precipitated by loud noises. These were captured on EEG on day 2 of life which demonstrated brief tonic seizures as well as epileptic spasms. EEG background showed bihemispheric phase reversing epileptiform transients. Lactate was initially raised at 5.9 but subsequently normalised. Extensive metabolic investigations and MRI brain were normal. CSF was not suggestive of infection. On examination the baby appeared to have hypertonia and glabellar tap elicited typical episodes. The Vigevano manoeuvre led to immediate abolition of typical episodes. A repeat EEG on day 9 of life showed a more continuous background with multiple brief tonic episodes caught whilst asleep and awake with no epileptiform correlate. The EEG pattern was still not typical of hyperekplexia. Initiation of clonazepam led tonic episodes resolving and normalisation of tone. Whole exome sequencing (WES) detected a likely pathogenic variant of GLRA1 NM_001146040.1: c.736C>T Chr5: g.151231127G>A p.(Arg246Trp) consistent with a diagnosis of hyperekplexia.

Conclusions: Our case highlights that epileptic seizures can co-exist with hyperekplexia leading to potential misdiagnosis. However, such significant EEG abnormalities have not previously been reported in association with hyperekplexia. The typical EEG findings are fast spikes during tonic spasms and then eventual flattening which were not demonstrated in our case. Careful clinical examination of the baby led to the clinical suspicion of hyperekplexia whereas initial EEG favoured an epileptic encephalopathy. Due to a broader differential diagnosis a gene agnostic approach was thus felt more appropriate which led to the eventual diagnosis.

Poster No. 093

LAS1L missense variant with clinical response to Riboflavin: A case report

J RAPER[3], R RICHARDSON[2], M MCKEAN[4], AP BASU[1,3]

[1]Population Health Sciences Institute, Newcastle University, Newcastle upon Tyne, UK; [2]Institute of Genetic Medicine, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; [3]Paediatric Neurology, Great North Children's Hospital, Newcastle upon Tyne, UK; [4]Paediatric Respiratory Medicine, Great North Children's Hospital, Newcastle upon Tyne, UK

Introduction: LAS1L variants have been identified in Wilson-Turner syndrome (WTS) and more recently Spinal Muscular Atrophy with Respiratory Distress (SMARD) type II. We present a patient with an LAS1L variant with features of both WTS and SMARD with an apparent clinical response to riboflavin supplementation.

Case: A 2 day old term neonate born in good condition after an uncomplicated pregnancy was transferred to PICU due to apnoeas. Examination revealed central hypotonia, head lag, weak cry and poor suck but preserved antigravity movements and reflexes. He had micropenis and an empty right hemiscrotum with hypogonadism. Biochemistry, MRI head, EEG, genetic tests for spinal muscular atrophy, Prader–Willi syndrome, and congenital myotonic dystrophy were normal. A sleep study showed central and obstructive apnoeas. By 3 months the patient had made no developmental progress and remained dependent on BiPAP and naso-gastric tube feeding. Tongue fasciculation was noted. EMG/NCS showed absent CMAP responses. Following high dose riboflavin supplementation (for possible riboflavin transporter deficiency/BVVL) there was marked improvement in tone and posture. He began oral feeding, was weaned from BiPAP and showed slow developmental progress though has since developed a severe epileptic encephalopathy. Repeat NCS was normal. Genetic testing for BVVL was negative but riboflavin supplementation was continued. Trio-whole-exome sequencing identified that he was hemizygous for a likely pathogenic LAS1L missense variant.

Discussion: LAS1L is an X-linked gene involved in ribosome biogenesis. How changes in the gene lead to the reported phenotypes is not understood. Our patient displays an intermediate phenotype between SMARD type II and WTS. The response to riboflavin remains unexplained though may be a nonspecific antioxidant effect and merits further investigation.

Poster No. 094

A case report of TRAPPC12-related severe developmental delay, microcephaly, spasticity and seizures with MRI findings of abnormal corpus callosum, pons hypoplasia and diffuse atrophy

V CURRIGAN[1], R RICHARDSON[2], D MITRA[3], A BASU[1]

[1]Paediatric Neurology, Great North Children's Hospital, Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK; [2]Genetics, Centre for Life, Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK; [3]Neuroradiology, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK

Case report: A female infant was born via caesarean section at 31 weeks due to poor fetal growth and history of a previous pregnancy resulting in intra-uterine death of a baby noted to have short limbs. This infant also had short limbs and continued to have faltering growth, length and head circumference below the 0.4th centile despite nutritional intervention. The neonatal period was complicated by Klebsiella meningitis. She had severe dystonia, myoclonic seizures, cerebral visual impairment and feeding difficulties leading to gastrostomy insertion. There has not been evidence of neurodevelopmental progression with age to date (she is now 2 years old). MRI head showed atrophy of the corpus callosum with an abnormal brainstem, flattened pons. Trio whole exome sequencing identified that she was compound heterozygous for a likely pathogenic TRAPPC12 nonsense variant and a TRAPPC12 missense variant of uncertain significance. TRAPPC12 is not currently included in the Epilepsy gene panels available in the UK NHS services.

Discussion: Trafficking protein particles (TRAPP) complexes function in membrane trafficking from the endoplasmic reticulum to and through the Golgi body. 3 children from 2 unrelated families have previously been described with biallelic TRAPPC12 variants with a strikingly similar phenotype to our patient, including severe developmental delay, microcephaly, spasticity with characteristic findings on MRI of corpus callosum abnormalities with pons hypoplasia and diffuse brain atrophy. Fibroblasts from those individuals showed fragmented Golgi that could be rescued by expression of wild-type TRAPPC12. Functional work on fibroblasts derived from our patient is ongoing in order to clarify the significance of these variants. Ongoing research aims to identify the precise function of this gene which may in turn lead to treatment options. This case report highlights the clinical and radiological findings that appear to be typical in TRAPPC12- related disorder.

Poster No. 095

Long-term neurological outcome of term-born children treated with two or more anti-epileptic drugs during the infantile period

R MUKHERJEE

IAP, Mumbai, India

Objective: To notice the progress of neurological compromise of those children who had to undergo medication with more than two AED for prolonged period from 3 to 6 months of age and keep a surveillance on them.

Methods: We included 94 children (born between 2014–2018) treated for neonatal seizures. We recorded mortality, aetiology of seizures, the number of AEDs required, achievement of seizure

control, and amplitude-integrated-EEG (aEEG) background patterns. Follow-up consisted of an age-adequate neurological examination. Surviving children were classified as normal, having mild neurological abnormalities, or cerebral palsy (CP). Forty-eight infants (51%) had status epilepticus. Initially after the first episode of convulsion single anti-epileptic drug started but had to add the second one very soon due to poor control. In a significant number of cases (36%) add on 3rd drug started within 6 months of the second. The worst part was 4th drug added desperately to stop seizure in (24%).

Results: The number of AEDs was not related to neurological outcome. Treatment with three or four AEDs as opposed to two showed a trend towards an increased risk of a poor outcome, i.e., death or CP. Failure to achieve seizure control increased the risk of poor outcome. Persistently severely abnormal aEEG background patterns also increased this risk. The sequelae were noted after a minimum of 3 months of start of 3rd/4th drug. The study period was for 9 months in between, 4 of them ceased to survive. Statistically the highest number was seen to be Spastic CP 38 (42%) followed by flaccidity 22 (24%). Next was Global Developmental Delay 16 (17%). The rest of the cases were divided into Movement or coordination disorders with sporadic Autism Spectrum (3/4). There were two syndromes: lihe Sturge weber and Tuberous Sclerosis.

Conclusion: In term-born infants with seizures that required two or more AEDs outcome was poorer if seizure control failed.

Poster No. 096
Multiple sulfatase deficiency, Austin disease case report

C BOUBIDI, AM BENMANSOUR, Z ZEROUAL
"A" CHU Hussein Dey Algiers, Hussein Dey, Algeria

Introduction: Multiple sulfate deficiency (MSD), is a very rare disease combining features of mucopolysaccharidoses (MPS) and metachromatic leukodystrophy (MLD). Mutations of SUFM 1 (sulfatase modifying factor) gene leads to defective for mylglycine-generating enzyme (FGE) which activates the different sulfatases.

Case report: SB boys patient, 4 years old of consanguineous parents 2° was referred of mental retardation with bone deformities; no other patient in both maternal and paternal families. At 9 months, the parents remarked the developmental delay, and sought medical attention in a hospital. General palsy was the initial diagnose and the patient was referred to a rehabilitation center. At 4 years, a physician referred the patient to our hospital.

On examination: General appearance: coarse hair, harsh eyebrows, coarse facial features, short neck, claw hands, ichthyosis, angiokeratomas, scaphocephaly, and hypertrichosis, liver and spleen were within normal range values. Joint limitations with genu varum and and Kyphoscoliosis. The neurological examination finds: axial hypotonia with hypertony of four limbs, absent tendon reflexes in lower limbs, raising suspicion of a lysosomal storage disease. Radiologic findings: bilateral coxa valga, ovoid vertebrae, MRI revealed T2 –hypersignal of the white matter near the occipital horns of the lateral ventricles. Urinary Glycosaminoglycans tested positive in Algeria. A sample of dried blood Spots were sent to Hamburg metabolic laboratory. In both samples sulfatases were markedly diminished: Iduronate-2-sulfatase 0 (0.02–0.25)mmol/spot21 h, Arylsulfatase B 0.03 (0.14–0.7) Mmol/spot/21H.

Conclusion: MSD is rare disease Diagnosis is suspected on clinical signs especially when MPS features are associated to MLD - like signs and Ichthyosis. Urinalysis reveal dermatan and Heparan sulfate and sulfatides. The confirmation of the diagnosis is made by the presence of low levels of sulfatases. Genetic confirmation may be done by the presence of mutations in the SUMF1 gene. No effective specific treatment is actually available for MSD. The treatment is only supportive.

Poster No. 096a
The use of an algorithm to identify potential patients with neurotransmitter disorders

E FOX[1], L SCHLUETER[7], V MEHTA[2], R MADHU[3], E WASSMER[4], R ARORA[6], T COX[5], E BALLINGER[5], L TOLAN[5], M RANCE[1]
[1]PTC Therapeutics Ltd, Guildford, UK; [2]Hull University Teaching Hospitals NHS Trust, Hull, UK; [3]Alder Hey Children's NHS Foundation Trust, Liverpool, UK; [4]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK; [5]OPEN VIE, Marlow, UK; [6]Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK; [7]PTC Therapeutics, Frankfurt am Main, Germany

Objective: Neurotransmitter disorders (NTDs) are accompanied by developmental and neurometabolic signs and symptoms generally manifesting in early infancy, however timely diagnosis of patients remains challenging.

Methods: We accessed deidentified patients' records (including diagnoses, clinical procedures, clinical specialty, and tariff codes) from the Hospital Episode Statistics (HES) database, covering all National Health Service (NHS) inpatient admissions in England, between April 2008 and May 2020. Patients with NTDs diagnosis (International Classification of Disease version-10 codes E708-E709) had their records extracted. Using machine learning and clinical expert inputs, patient's clinical codes were ordered by frequency and given scores between 1 and 5 based on the degree of association with NTDs. To help characterise potentially undiagnosed patients, those with a total score ≥53 were flagged in HES as potential NTDs; and the five most common codes were then used as selecting criteria.

Results: From data on 56 million individuals, 289 patients had a diagnosis of E708-E709, and 1,972 patients had a total score ≥53. In potential patients, the five most common codes were, in order: attendance to paediatric neurology (ICD10 code 421), epilepsy (G40*), dystonia (G24*), cerebral palsy (CP; G809) and hypotonia (P942). A subset of 76 potential patients had all five codes recorded, and 118 potential patients had four codes (all except CP).

Conclusions: An innovative machine learning approach using deidentified hospital records profiled potential patients with NTDs. The algorithm will be shared with NHS Trusts managing patients with a possible NTD to enable them to run the algorithm on their local data, identify the patients and then recall them for further counselling and tests if deemed clinically appropriate; potentially shortening the time to definitive diagnosis and enabling earlier intervention. Our methodology may apply to other underdiagnosed conditions and serve as a novel strategy to aid patient's identification.

Poster No. 097

The first UK and Ireland surveillance of Fetal Alcohol Syndrome: neurological manifestations in children <16 years of age

K JOHNSON[1], C VERITY[2], AM WINSTONE[2], R LYNN[3]
[1]Leeds Teaching Hospitals NHS Trust, Leeds, UK; [2]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [3]British Paediatric Surveillance Unit, Royal College of Paediatrics and Child Health, London, UK

Introduction: In 2018/19 the first surveillance of Fetal Alcohol Syndrome (FAS) in children in the UK and Ireland, was completed using the world renowned British Paediatric Surveillance Unit methodology. The study sought to determine the incidence of FAS, not the much more commonly diagnosed Fetal Alcohol Spectrum Disorder. The surveillance case definition required, in addition to growth failure and facial features, the presence of a structural or functional brain abnormality including: Microcephaly, Abnormal brain scan, Developmental delay/learning difficulties, Abnormal neurological signs.
Results: The 13 month surveillance period for this study ended late in 2019. There were 148 notification of which nine were duplicates. Of the 139 remaining cases, follow-up contact with reporting clinicians have been made for 113 (>80%); contact with the remaining 26 clinicians has not been possible. 46 notifications were subsequently withdrawn given they did not fit the case definition. Of the 67 submitted data forms 19 more were excluded leaving 48 probable/confirmed cases. Key results: <10% of children were living with their birth mother at the time of diagnosis. >80% of cases had a documented definite history of exposure to alcohol in pregnancy. All cases had structural and or functional brain abnormality; a wide range of functional brain abnormalities were described and reported in all cases. Where information was available at birth >60% had microcephaly, this had risen to >80% at the time of diagnosis.
Conclusions: This study demonstrates the significant neurological impact of Fetal Alcohol Syndrome.
There is a lack of understanding of the FAS diagnostic criteria amongst paediatricians in the UK.
Future projects include surveillance for and understanding the neurological impact of FASD; known to be a much more common condition with equally significant associated neurological impairment.

Poster No. 098

Experiences of families with children with neurodisability during the Covid 19 pandemic restrictions.

ACN NETTLETON[1,2], CAB BODEY[2], CS SHEAHAN[2]
[1]Paediatrics, Bristol Royal Hospital for Children, Bristol, UK; [2]Community Child Health, Sirona Care and Health, Bristol, UK

Objectives: To understand the effects of the restrictions due to the COVID19 pandemic on children with disabilities and their families to enable us to better support them.
Methods: Purposive sampling of families of children with neurodevelopmental disabilities with semi-structured questionnaires delivered by telephone interview regarding their experience of lockdown (March–July 2020). These were transcribed contemporaneously and results were analysed thematically.
Results: Eleven interviews took place. 64% white British, 27% children <11 years. A number of themes emerged: service restriction, physical and emotional health, impact on family functioning, education, and preference for service provision post lockdown. Children's access to therapy was significantly impacted with 78% of children not receiving their usual therapy. Access to GP, hospital appointments and therapy was delayed or stopped, medication was difficult to obtain, respite was unavailable. Both children's physical and emotional health were negatively affected including increase in spasticity, appetite changes, mood disturbance, behaviour difficulties and regression in toileting and sleep. Adults also reported negative emotional impacts, some recognised positives. 70% of children did not attend education during the pandemic despite being in the vulnerable category. Preferences for restoration of services were spread over telephone, face to face, home visits and video consultations.
Conclusions: This group were adversely impacted by the lockdown restrictions by changes in our service as well as more generally. When redesigning our service, the needs and wishes of families must be considered. The children on our caseload are vulnerable and require input from multiple professionals to meet their diverse needs. The COVID 19 restrictions had a negative impact on services our children received and on their emotional and physical health and the well-being of their families. This must be considered when future lockdown plans are made.

Poster No. 099

Quantitative and qualitative adaptive level profiling at time of 1st diagnosis in children with autism spectrum disorder (ASD) to identify most affected functional domain

DV JAIN
Developmental Pediatrics, Shishu Child Development and Early Intervention Centre, Ahmedabad, India

Objective: ASD is one of the most prevalent neurodevelopmental disorders in children with current incidence of 1:54. It encompasses Social Communication delay along with restrictive and/or repetitive behaviour pattern and interest. Functionally children with ASD have delay in their adaptive levels, i.e. the skills child needs for selfcare and to function in society. This study attempts to examine adaptive level of children at the time of 1st diagnosis of ASD.
Method: This cross-sectional study was done in 84 children under 5 years of age with presentation of ASD on DSM-V criteria. VINELAND-III scale, a norm-based instrument was administered to compare the child's adaptive level to same age neurotypical children. Overall adaptive level and individual adaptive level in 4 domains- Communication, Daily Living Skills, Socialization and Motor Skills were assessed. Quantitative assessment was done as Percentile and Standard Score and Qualitative descriptors (low, moderately low, adequate, moderately high, high) were assigned to score bands.
Result: The mean age at 1st presentation was 2.97 years. In the Communication and Socialization domains the mean adaptive level was Low (2nd or <2nd centile) with standard score of 53.89 in Communication and 67.93 in the Socialization domain. In the Daily Living Skills and Motor domains the mean adaptive level was Moderately Low (3–17th centile) with standard score of 76.30 and 82.96 respectively. The overall adaptive level was Low with

mean standard score of 65.93. Communication domain was overall most severely affected.
Conclusion: The study indicates significantly low adaptive level in Communication and Socialization domain at time of first diagnosis. As Motor and Daily Living skills are less severely affected, parents may miss early warning signs of ASD leading to delay in diagnosis and intervention. It is important to introduce universal screening and to sensitize parents regarding warning signs at well baby visits in infancy to avoid delay in diagnosis.

Poster No. 100

Potential association between Ov16 seropositivity and neurocognitive performance among children in rural Cameroon: a cross-sectional study

JN SIEWE FODJO[1,5], WY NJAMNSHI[1,2], C AYUK[2], HT EKWOGE[3,4], R COLEBUNDERS[5], AK NJAMNSHI[1,2]
[1]Brain Research Africa Initiative (BRAIN), Yaoundé, Cameroon/Geneva, Switzerland; [2]Faculty of Medicine & Biomedical Sciences, The University of Yaoundé I, Yaoundé, Cameroon; [3]Buea Regional Hospital, Buea, Cameroon; [4]HILPharma Organization, Yaoundé, Cameroon; [5]Global Health Institute, University of Antwerp, Antwerp, Belgium

Introduction: Infection with Onchocerca volvulus was recently reported to increase the risk for epilepsy in Cameroonian children. Moreover, cognitive impairment is frequent in children with onchocerciasis-associated epilepsy (OAE). We investigated whether infection with O.volvulus may affect cognitive performance in children who may or may not develop OAE later in their lifetime.
Methods: A community-based study was conducted in three onchocerciasis-endemic villages in Cameroon between August 2019 and January 2020. We recruited school-aged children without epilepsy, and investigated exposure to O.volvulus by testing for Ov16 antibodies using rapid diagnostic tests. The neurocognitive performance of enrolled children was assessed using locally validated tests (Purdue Pegboard Test, Hand Movements, Semantic Verbal Fluency Test, Digit Span) as well as paediatric adaptations of other well-known cognitive assessment tools (mini-mental state exam, and the International HIV Dementia Scale).
Results: Overall, 209 children aged 6 to 16 years were included in the study; 46.4% were Ov16 seropositive. When 5th percentile cut-off values were used to dichotomise neurocognitive scores into normal vs below normal, there were no significant differences in cognitive performance between Ov16-positive and Ov16-negative children. Upon standardizing age-specific neurocognitive scores and investigating predictors of neurocognitive performance using multiple linear regression models (adjusted for gender, education level, previous ivermectin use, and anthropometric parameters), we found that being Ov16-positive was significantly associated with reduced semantic verbal fluency (Estimate: –0.38; 95% confidence interval: [–0.65 to –0.11]; p=0.006) and lower scores on the International HIV Dementia Scale (Estimate: –0.31; confidence interval: [–0.56 to –0.04]; p=0.025). Furthermore, more intakes of ivermectin (drug to treat onchocerciasis) in the past was associated with increased neurocognitive scores.
Conclusion: Our findings suggest that infection with O.volvulus may affect neurocognitive performance of children. Larger studies with a longitudinal design are warranted to confirm these preliminary observations.

Poster No. 101

Efficacy and safety of incobotulinumtoxinA in the treatment of children and adolescents with chronic troublesome sialorrhea associated with neurological disorders and/or intellectual disability

S BERWECK[1], M ALTHAUS[2], A HANSCHMANN[2]
[1]Schoen Klinik Vogtareuth, Vogtareuth, Germany; [2]Merz Pharmaceuticals GmbH, Frankfurt am Main, Germany

Phase III, prospective, randomized, double-blind, placebo-controlled, parallel-group, multicentre study with an open-label extension (OLEX) conducted at 28 sites in Europe and Russia. Children/adolescents (2–17 years) with chronic troublesome sialorrhea and/or intellectual disability associated with neurological disorders, and severe drooling (investigator's Modified Teacher's Drooling Scale rating ≥6), were recruited. 6 to 17 year olds were randomized 2:1 to receive ~2 U/kg body weight (BW) of incobotulinumtoxinA (fixed total dose 75U for participants ≥30kg BW) or matching placebo in the main phase (MP). Participants aged 2 to 5 years were treated only with incobotulinumtoxinA. All participants received 3 further incobotulinumtoxinA injection cycles (IC) according to the above-mentioned weight-adjusted dosing scheme. The co-primary efficacy endpoints were unstimulated Salivary Flow Rate (uSFR) change from baseline to Week 4 and carer's Global Impression of Change Scale (GICS) score at Week 4. The change in uSFR from study/cycle baseline to Weeks 4 and 16 and GICS score at Weeks 4, 8, 12 and 16 of each OLEX cycle, and the occurrence of treatment-emergent adverse events (TEAEs) overall and by injection cycle, were also assessed. 256 participants were randomized, 250 (97.7%) completed the MP. 247 participants entered the OLEX, of which 222 (89.9%) completed all 3 ICs. The treatment group showed a statistically significant superiority over placebo in both uSFR change from baseline to Week 4 and improvement in carer's GICS score at Week 4. Improvement in uSFR and carer's GICS score was observed over the course of the OLEX with a cumulative effect after repeated incobotulinumtoxinA treatment. Both MP and OLEX had good overall safety profiles. No major differences were observed in TEAE incidence between groups in the MP, and TEAEs did not increase with increasing number of ICs. IncobotulinumtoxinA is effective and well tolerated for the treatment of children and adolescents with chronic troublesome sialorrhea.

Poster No. 102

UK paediatric neurorehabilitation in a time of Covid-19: A guide to rebuilding sustainable services

PM SHARPLES[1], J WILLIAMS[2]
[1]Bristol Royal Hospital for Children, Bristol, UK; [2]Nottingham Children's Hospital, Nottingham, UK

Objective: The Covid-19 pandemic poses significant concerns for children with neurological problems and many challenges for clinicians trying to deliver high quality care. Evidence from a BPNA Neurorehabilitation Network survey shows neurorehabilitation has been particularly negatively impacted. We aimed to produce a Guideline to assist UK clinicians, providers and Commissioners, including regional neuroscience centres, where most paediatric neurorehabilitation is undertaken, in rebuilding sustainable specialist neurorehabilitation services.

Methods: The proposal to produce a Guideline was put to BPNA Neurorehabilitation Network members at a virtual meeting on 9 June 2020 and supported. A draft Guideline was produced and circulated to all members of the Network and NHS England Paediatric Neuroscience CRG Neurorehabilitation sub-group. A final draft was developed, with input from Network and CRG members, and submitted for endorsement to the BPNA Executive.
Results: Key recommendations include: (1) neurorehabilitation beds must be provided for children who cannot be safely discharged and/or need to access inpatient rehabilitation services in the post-acute period; (2) centres should be able to offer "step down" specialist neurorehabilitation, on an outpatient or outreach basis, to medically stable children who can be safely discharged from hospital, to reduce length of stay while maintaining recovery trajectory; (3) appropriate outcome measures should be used to check recovery continues post-discharge to outpatient/outreach services; (4) close joint working between regional neurorehabilitation and district community teams ("Hub and Spoke" model) to ensure a smooth patient pathway and ongoing support to children and families post-discharge. Telemedicine will facilitate joint working; (5) use of virtual measures to teach and to promote safe interaction between children, while consideration is given to developing ways of safely allowing face to face teaching and small group activities.
Conclusion: The opportunity exists to create a responsive, efficient, equitable and resilient quality model of neurorehabilitation for children with acquired neurological disorders.

Poster No. 103
Improving data integrity and quality through the implementation of an institutional patient registry – experience with cerebral palsy

SC ALDRIDGE[2], L ROBERTS[1], S LANES[1], O PEATMAN[1], J CADWGAN[2], C FAIRHURST[2], DE LUMSDEN[2]
[1]Department of Clinical Coding, Evelina Children's Hospital, Guy's and St Thomas' Foundation Trust, London UK; [2]Department of Paediatric Neurosciences, Evelina Children's Hospital, Guy's and St Thomas' Foundation Trust, London, UK

Objectives: Condition-specific patient registries are a foundation for understanding disease manifestation and processes, as well as important drivers for care pathway redesign, real-time analytics and quality improvement. Cerebral palsy (CP) is the most common cause of physical disability in children and young people, so is an exemplar choice for a registry.
Aims: (1) Assess the accuracy and consistency of CP, and associated chronic conditions, in clinical documentation. (2) Explore the potential benefits of a register to improve data capture and accuracy.
Methods: A consultant-validated CP registry, documenting the ICD-10 phenotype of CP, Intellectual Disability (ID), Epilepsy (EP), Hearing Impairment (HI) and Visual Impairment (VI) was created. Discharge Letters (DL), Electronic Health Records Diagnosis Lists (EHRD) and Clinic Letters (CL), completed within the 6 months prior to discharge were reviewed of registered patients, discharged January 2019 to April 2020. Comparison to the register was made and categorised as: Indistinct Phenotype (IP), Incorrect Diagnosis (IncD), Absent Diagnosis (AD). Results were analysed, and clinical coding was amended by a qualified clinical coder. Financial benefits were quantified.
Results: The study cohort consisted of 57 patients, with 184 documents (DL: 31; EHRD: 34; CL: 119). Spell discharge documentation was absent in 26 cases (45.6%). The total categorical error distribution was: IP: (14.0%); IncD: 29 (4.2%); AD: 261 (38.1%). EHRD had the highest overall error rate, across the documentation types, at 81.3% (100/123). ID was the most regularly missed diagnosis (DL: 26 [89.7%]; EHRD: 27 [84.4%]; CL: 120 [69.4%]); CP had the most frequent phenotypical issue (DL: 10 [32.3%]; EHRD: 19 [55.9%]; CL: 62 [33.7%]). A financial benefit of £45,400 was recognised through clinical coding amendments.
Conclusions: Inconsistent clinical documentation in this CP population was common, and may negatively affect disease management. Registers provide a sustainable mechanism for ensuring data consistency, reliability and interoperability.

Poster No. 104
Yield of diagnosis in MRI brain imaging in children with autism spectrum disorder

D BYRNE[1], KM GORMAN[2,3], E TWOMEY[4], L BAKER[1]
[1]Department of Neurodisability, CHI at Temple Street, Dublin, Ireland; [2]Department of Paediatric Neurology and Clinical Neurophysiology, CHI at Temple Street, Dublin, Ireland; [3]School of Medicine and Medical Sciences, University College Dublin, Dublin, Ireland; [4]Department of Radiology, CHI at Temple Street, Dublin, Ireland

Objective: The prevalence of autism spectrum disorder (ASD) in Ireland is approximately 1.5%. Guidance from the American Academy of Paediatrics (AAP) and American Academy of Neurology (AAN) suggest routine magnetic resonance imaging (MRI) brain imaging is not part of the initial work up of diagnosing ASD. The AAP also state the consensus on the role of neuroimaging in the evaluation of children with global developmental delay or intellectual disability is unclear. Our *Objective:* was to identify the yield of MRI brain in children with ASD, in whom MRI was performed as part of investigations for their presentation with ASD.
Methods: Indications for MRI brain were searched over a 5 year period on our radiology system using key words (ASD, autism, autistic and spectrum). Only MRI brain performed for the work-up of ASD were included.
Results: 210 MRI brains were identified. 29 were excluded due to a known medical diagnosis (19), or prior brain insult (10). 181 MRI brains were included in analysis. 84% were done under general anaesthetic. Reasons for imaging included ASD and possible diagnosis of epilepsy (65), ASD and developmental delay (30), ASD with no other indications for MRI (28), ASD and behavioural changes (20), ASD and developmental regression (17), ASD and focal neurological findings (8), and ASD with other indications (13). In total 2.2% (4) had clinically significant findings. In children with ASD and no other indications there were no clinically significant findings.
Conclusion: This study highlights the low yield of routine MRI brain in children with ASD (2.2%). Previous studies have shown similar results on the utility of MRI. 75% of clinically significant findings were in those with focal neurological findings. MRI brain should be considered in children with acute regression, microcephaly, midline facial defects, neurocutaneous lesions, or focal neurological findings according to AAP guidelines.

Poster No. 105

Management of pain and sleep difficulties in children with cerebral palsy – a quality improvement audit

E BROWN[1], H PALANYIAYA[1], A RAJESH[2]
[1]Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, UK; [2]Norfolk Community Health and Care NHS Trust, Norwich, UK

Objectives: Children and young people with Cerebral Palsy commonly experience difficulties with pain and sleep. The NICE guidelines on 'Cerebral Palsy in under 25s' recommend that pain and sleep difficulties are assessed and addressed at each clinical encounter, therefore we sought to improve our compliance to these standards using a quality improvement audit cycle.
Methods: An audit of our practice in the Multidisciplinary Cerebral Palsy clinic in 2018 demonstrated poor compliance with NICE guidelines, therefore a pain assessment tool for non-verbal patients and a clinic proforma were introduced in order to standardise care. A prospective re-audit of all patients seen in the Cerebral Palsy MDT clinic was carried out over a 6 month period in 2019.
Results: Re-audit showed excellent compliance with pain assessment, increasing from 50% to 98% of patients. The cause was considered in 93% of those with pain, rising from 78%. 86% of those with pain received pain management plans, increasing from 15%. 39% of non-verbal children's carers perceived them to have pain and the assessment tool was only employed in these cases. Using a clinic proforma improved the assessment of sleep difficulties from 63% to 98%, with 87% of patients receiving a clear management plan for sleep difficulties.
Conclusions: The audit cycle demonstrated significant improvement in multidisciplinary care of pain and sleep difficulties, in line with national standards. Onward recommendations include using a pain assessment tool for all non-communicating patients, even if pain is not identified by carers at initial assessment. We also encourage consistent provision of sleep and pain management plans, including a step-wise analgesic approach, where difficulties are identified.

Poster No. 106

Audit of acquired spinal cord injury outpatient management- outcomes and recommendations

MJ ATHERTON[1], D ROWLEY[2], S HEWITT[3], E DAVIES[1]
[1]Department of Paediatric and Neonatal Neurology, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK; [2]Department of Paediatric Physiotherapy, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK; [3]Department of Paediatric Orthotics, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK

Objective: To review the outpatient management of children with acquired spinal cord injury (ASCI) in a tertiary children's centre against national standards. Secondary analysis compared outcomes in a new specialist multi-disciplinary team (MDT) clinic versus routine outpatient follow-up.
Methods: A retrospective audit was conducted including all patients with an ASCI under current follow-up in our Trust, which provides tertiary paediatric services to Sheffield and the surrounding region and has affiliation with a specialist spinal injuries centre. Management was audited against the NHS England Service Standards (2014) for children aged under 19 years requiring spinal cord injury care, including appropriate follow-up and transition care, MDT involvement, and appropriate review of clinical criteria as stated within the Standards of Care.
Results: All 24 patients currently under the active care of our Trust with a coded diagnosis of ASCI were included. Diagnoses included traumatic and non-traumatic (e.g. demyelinating disorders, spinal stroke and spinal cord tumours) ASCI. 13/24 patients were reviewed in a new specialist MDT clinic with the remainder seen in separate paediatric neurology or oncology clinics. All patients were seen within the past year by a physiotherapist (where appropriate), 20/24 by a paediatric neurologist, 17/24 by an orthotist (where appropriate), 14/24 by paediatric urology, 12/24 by a spinal injury consultant, and 10/24 by a spinal surgeon. Documented assessment of height, weight, blood pressure, spine growth, Vitamin D level, hip surveillance, autonomic dysreflexia and family outcome measures were commonly missed in clinic, particularly in those not under the care of the specialist MDT clinic.
Conclusions: Children with ASCI received improved care as measured against national standards when seen in a specialist MDT clinic. Key aspects of management include measurement of growth parameters, assessment of the hips and spine, discussion of autonomic dysreflexia in at-risk patients, and review of urological and respiratory function.

Poster No. 107

Development of a core outcome set for lower limb surgical interventions in ambulant children with cerebral palsy

H ALMOAJIL[1,2], H DAWES[3,4], S HOPEWELL[1], F TOYE[5], T THEOLOGIS[1,6]
[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK; [2]Department of Physical Therapy, College of Applied Medical Science, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia; [3]Centre for Movement, Occupational and Rehabilitation Sciences, OxINMAHR, Oxford Brookes University, Oxford, UK; [4]Oxford Health NHS Foundation Trust, Oxford, UK.; [5]Physiotherapy Research Unite, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [6]Paediatric Orthopaedic Surgery, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Objective: The objective of our study was to develop a core outcome set for ambulant children with cerebral palsy and lower limb surgical interventions.
Methods: To generate a list of categorised outcomes for inclusion in the eventual core outcome set (COS), a set of outcomes domains and outcome measures were developed from (1) qualitative evidence synthesis to surgical experiences and expectations from children and family perspective; (2) scoping review to identify reported outcomes and outcome measures; (3) qualitative research to explore what outcomes are important from health professionals, children and their family's perspective.
Results: There were 54 outcomes with substantial heterogeneity in their reporting. Some outcomes were reported in one study only. These findings demonstrated the need for a core outcome set. The 54 outcomes were assigned to 8 core outcome areas: pain and muscle soreness, physiological manifestations of CP, daily life activities, independence, mobility, social life, quality of life, and adverse events. There are substantial inconsistencies in the number and type of outcome measures across studies with a significant

focus on clinician-administered and measured musculoskeletal manifestations.
Conclusion: Outcomes identified through these studies will be used to help stakeholders prioritise outcomes and reach consensus on a COS for children with CP undergoing lower limb surgical interventions. These studies provide children and families guidance for the health outcomes that matter to children and should be considered for COS inclusion. The proposed COS aims to provide guidance for future lower limb surgical research and to inform clinical practice. This does not imply that primary outcomes should utterly be those of the COS. However, to enhance the comparability across study results, the outcomes included in this COS should be considered for inclusion in addition to measuring study-specific clinical endpoints. Further work is currently carried out in order to agree on how to best measure the outcomes included in this COS.

Poster No. 108
Cerebral palsy - what and why? Audit of the assessment and management of paediatric cerebral palsy within a children's hospital

A MICHAEL, G HYLIGER, D CROZIER, KRM MARTIN
Paediatric Neurodisability, Nottingham Children's Hospital, Nottingham, UK

Objective: To evaluate the assessment and management of children and young people (CYP) with cerebral palsy (CP) within Nottingham Children's Hospital (NCH), with reference to NICE guidance (spasticity and CP).
Methods: CYP with CP were identified using the Cerebral Palsy Integrated Pathway East Midlands database. Inclusion criteria: age 2 to <19 years, diagnosis of CP, registered with GP in Nottingham City or Nottinghamshire County South, notes available electronically to August 2020. Exclusion criteria: outside of age range, other diagnosis, GP outside specified areas, notes unavailable.
A standard pro forma was designed to capture information from electronic hospital records and correspondence including: use of Surveillance of Cerebral Palsy in Europe (SCPE) classification and Gross Motor Function Classification System (GMFCS), identification of aetiology, involvement of other relevant medical/surgical teams, use of tone modifying agents, surgery.
Results: 264 CYP were identified, of which 197 met the inclusion criteria. 188 (95%) were under follow-up by neurodisability/community paediatric teams, 31 (16%) by paediatric neurology. 127 (64%) had classification documented using SCPE terminology and 127 (64%) using GMFCS in the past 12 months. 91 (76%) of GMFCS ratings documented by paediatricians were in concordance with physiotherapists' ratings. 182 (92%) of CYP had aetiology documented at any time and 175 (89%) had had an MRI brain scan at any time. 44 (22%) had received oral medication for tone, 35 (18%) botulinum toxin injections and 22 (11%) both. 118 (59%) were known to orthopaedics; 41 (21%) had received orthopaedic surgery. 27 (14%) were monitored by spinal team; 2 (1%) had had scoliosis repair.
Conclusions: The vast majority of CYP with CP within NCH are managed by a child development service. Areas for improvement include accurate use of recognised terminology and classification systems. We have developed a clinic letter template to prompt best practice, improve documentation and facilitate re-audit.

Poster No. 109
Sleep deprivation and cognitive development in Down's syndrome

AR RENGIT
William Harvey Hospital, KMPT, Kent, UK

Objectives: Consider impact of sleep deprivation on cognitive development in Down's syndrome, including: Baseline cognitive function, Variation across cognitive domains, Risk of early cognitive deterioration.
Methods: Search terms used: (Child OR Paediatric OR Pediatric) AND (Sleep OR Insomnia OR Parasomnia) AND ((Downs AND Syndrome) OR (Trisomy AND 21)) AND ((Cognitive AND impairment) OR Intellect OR function OR Memory OR Learning OR Verbal OR Language). Literature reviewed across various research databases: (1) NICE HDAS - cross-sectional search across HMIC, AMED, Medline, BNI, PsycINFO, CINAHL, Pubmed, EMBASE & EMCARE databases; (2) Google Scholar; (3) Mendeley reference manager.
Results: Current research suggests that children with Down's syndrome are at higher risk of sleep deprivation compared to neurotypical children. This contributes to difficulties with attention, impulse control, memory formation and language development. Unfortunately, there is limited research on this topic - and studies often focus on Obstructive Sleep Apnoea as the primary sleep disorder, commonly found in Down's syndrome. In the studies evaluated, only one study commented on other sleep disorders, such as sleep anxiety or parasomnias. Across the literature reviewed, there was little consideration of confounding variables which can also impact cognitive development in Down's syndrome - such as the presence of co-morbid neurodevelopmental conditions, or seizure history.
Conclusion: There is a high degree of correlation between sleep deprivation and reduced cognitive development in Down's syndrome. It is notable that the cognitive domains affected, such as memory formation and language development can impact on both academic and social skills development. Therefore, more longitudinal research on the following issues may be beneficial to improving cognitive outcomes in children with Down's syndrome: (1) whether reduced baseline cognitive function secondary to sleep deprivation increases the risk of early cognitive decline in Down's syndrome; (2) the impact of early sleep intervention programmes on cognitive development in Down's syndrome

Poster No. 110
NFIB related neuro-developmental disorder with Infantile spasms, a unique presentation

PD DAVE, TSR TEKKIE-RAO
Luton and Dunstable Hospital, Luton, UK

Background: Nuclear Factor 1B (NFIB) haploinsufficiency is associated with intellectual deficiency (ID) and macrocephaly. All individuals present with additional variable neurodevelopmental phenotypes including muscular hypotonia, motor and speech delay, ADHD, autism and behavioural abnormalities. In 2018, Ina Schanze et al reported in the American journal of human genetics that NFIB mutations as causative for ID. Although congenital malformations and facial anomalies that allow clinical recognition of the disease, they are not part of the presentation. All

individuals share some minor dysmorphic features. Epilepsy was not described in this genetic disorder. We present a rare case of NFIB disorder who developed infantile spasms.
Case presentation: A 5-years old girl with mild developmental delay, mild learning difficulties and macrocephaly at 1 year of age also presented with infantile spasms from the age of 7 months. She developed epileptic encephalopathy with regression of milestones. 100,000 genomes showed pathogenic NFBI gene variant. She was a term baby born via forceps delivery, to non-consanguineous parents. Antenatal nuchal screening in early pregnancy showed increased thickness and chorionic villous biopsy undertaken, showed trisomy 8 mosaicism. Postnatal karyotype and microarray were reported normal. Phenotype includes frontal bossing with visible veins, depressed nasal bridge, epicanthic fold, nuchal angioma, normal ears, deep palmar creases, generalised hypotonia, normal reflexes and macrocephaly. Cranial ultrasound and MRI head were normal.
Conclusion: This is a relatively newly recognised genetic condition with only 18 patients described in medical literature and epilepsy is not a reported feature. Thus, this case is varied from other individuals in that she presented with infantile spasms which adds to the phenotype of NFIB.

Poster No. 111
Triggered episodes in Angelman syndrome

D HINDLEY[1], Z YUSUF[1], J CLAYTON-SMITH[2]
[1]Community Paediatrics, Bolton NHS Foundation Trust, Bolton, UK; [2]Genetics, North West Regional Genetic Service, St Mary's Hospital, Manchester, UK

Triggered episodes are recurrent unusual episodes in response to external stimuli or emotion that may have a neurological, cardiovascular, or behavioural cause. Such episodes occur in Angelman syndrome and are poorly understood. To better understand these episodes we asked families to report triggered episodes via the Angelman UK national support group. We received responses from nine families describing triggered events for nine patients (four male and five female) aged 4 years to 24 years. Triggers included dressing, travelling in cars, eating, laughter, and toileting. The events included loss of tone, vacant and blinking episodes, head nods, and stiffness and cramping of the hand. Some triggered events resulted in falls and injuries, while others were associated with poor seizure control. Some families reported reduced events with distraction techniques or trigger avoidance. Most families reported that few investigations had been done to understand the cause and no diagnosis or explanation had been given. To further understand triggered episodes it would be helpful to view videos of typical events and, if possible, to capture a provoked event during investigations such as video electroencephalography. Further review of triggered episodes may clarify the aetiology and raise potential treatment options that could improve the quality of life of people with Angelman syndrome and their families.

Poster No. 112
Developmental outcomes at 2 years for babies born at our hospital at less than 32 weeks gestation or less than 1501 grams compared to Epicure study and the Badger system

SSK DHULIPALA, N MADDOCK
Royal Oldham Hospital, Oldham, UK

Background: Developmental follow up can be at any time between 22 months corrected gestational age and 3 years chronological age but the data has to be uploaded onto the Badger to meet the National Neonatal Audit Programme requirement.
Aims: This audit will look to see that we offer all patients follow up, how we manage patients who fail to attend the follow up appointments and look at this over time to make sure any previous changes have improved the follow up until 2 years corrected age. To compare our outcomes against National statistics of Epicure study. To compare our compliance with the requirement to complete follow up and to see how we compare with the national data.
Methods: Babies born at Royal Oldham hospital at less than 32 weeks gestation at birth or with a birth weight of less than 1501 grams and who have their third birthday between 1 January 2015 and 31 March 2019. There were 333 cases identified. Information was obtained from Badger and the automated letter system.
Results: Preterm survival and outcomes are in line with the national statistics. All babies who failed to attend their first appointment, were offered a second appointment. Reason for not offering a second appointment was clearly documented when a second appointment was not deemed appropriate. Standardised approach and standardised tool were used when seen at 2 years. Documentation on Badger when the children were seen needs improvement.
Recommendations: Improve developmental follow up appointment attendance by providing information leaflet parents about the importance of 2 year follow up. Annual re-audit.

Poster No. 113
Reminder of potential for long term improvement following severe TBI in childhood

MR SMITH[1], E GLISSON[1], C BEAUMONT[1], C JONES[1], A MYHILL[1], C EVANS[1], K SCARFF[1], S CHOWDHURY[1], R BUTLER[2], A MAW[3], A CALISTO[1], T LAWRENCE[1], G COSTELLO[4], M KENNEDY[4], R VITHLANI[4]
[1]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]Health and Case Management Ltd, Croydon, UK; [3]Addenbrookes Hospital, Cambridge, UK; [4]The Children's Trust, Tadworth Court, Surrey, UK

An 11 year old male sustained a severe traumatic brain injury (TBI) in a RTA. He received standard neuro-protective measures, but did not undergo decompressive craniotomy. One month following the injury he was unable to maintain his own airway, and was showing no consistent signs of responsiveness to external stimuli. There was a range of views on whether to prolong life with tracheostomy placement +/- ongoing ventilator support, or switch to a palliative approach due to concerns that continuation of invasive medical therapies would prolong suffering and/or he would be unable to derive benefit from prolonged survival. However, a final attempt at extubation was successful, and he received

ongoing rehabilitation. Assessment of recovery of consciousness was monitored via weekly performance of the JFK Coma Recovery Scale – Revised (CRS-R). This consists of 23 items within 6 sub-scales addressing auditory, visual, motor, oromotor, communication and arousal functions. The lowest item on each subscale represent reflexive activity while the highest items represent cognitively-mediated behaviours. Scores were 6 and 15 after 6 weeks and 9 months respectively. At 16 months post TBI the key points of his condition include: Asymmetrical motor disorder (spasticity and dystonia), but able to sit independently on a plinth, and partially roll; Non-verbal but able to use yes/no switches and eye pointing; Partially orally fed; Reported to be settled and happy.
Discussion: This case illustrates the common dilemma faced by family and professionals in determining best interests following severe TBI, but emphasises that following TBI there can be very prolonged recovery of consciousness. Our patient has been left with severe neurodisability and will require full time care for the remainder of his life. However, the concerns that he would inevitably be exposed to a high level of suffering or be unable to perceive benefit have not transpired.

Poster No. 114
Review of perinatal stroke in Cork University and Maternity Hospitals over a 10-year period

C TERRY[1], N MCSWEENEY[1], P FILAN[2]
[1]Department of Paediatric Neurology, Cork University Hospital, Wilton, Co Cork, Ireland; [2]Department of Neonatology, Cork University Maternity Hospital, Wilton, Co Cork, Ireland

Introduction: Perinatal stroke is a cerebrovascular event (ischaemic, haemorrhagic or venous sinus thrombosis) occurring between 20 weeks gestation and up to 28 days after birth. Significant long-term morbidity is associated, highlighting the importance of early recognition and management.
Objectives: To describe our experience of perinatal stroke over a 10-year period (2010–2019) in a tertiary centre.
Methods: Retrospective observational study of infants identified in Cork University and Cork University Maternity Hospitals.
Results: Thirty-three term infants with perinatal stroke were identified with male predominance (63%). 29 (85%) presented in the first 48 hours with 26 presenting with focal seizures at a mean age of 17.3 hours. One had focal seizures at 49 hours. 8 had refractory seizures (requiring more than one anticonvulsant). Risk factors such as maternal preeclampsia, chorioamnionitis, maternal prothrombotic disorders and meconium stained amniotic fluid were identified in 17/33 patients (51%). MRI identified ischaemic infarction in 26/33 (79%); of which 12/26 (46%) had involvement of left middle cerebral artery territory, Haemorrhage 4/33 (12%) and Venous sinus thrombosis in 3/33 (9%). EEG on 23/29 patients showed suppressed background predominantly over the affected side. Frequent focal sharp waves were recorded in 9 patients. 20/33 had an ECHO performed. Thrombophilia screen was performed on 11/33 patients and was normal in all cases. Placental histology was available in 3/33 cases and all had features of fetal vascular malperfusion. Follow up data (mean follow up 2.8 years) was available on 26/33 patients. Motor outcome was normal in 15/26 (58%) patients. Hemiplegia was present in 11/22, 5 had cortico-visual impairment. 6 had cognitive impairment. Three patients had focal epilepsy.
Conclusions: We report a similar prevalence of 1 in 2,500 live births as that reported in the literature. Focal seizures in the first 24 hours are highly predictive of perinatal stroke. Outcomes were variable with 42% having motor impairment, 23% cognitive impairment and 19% with visual impairment.

Poster No. 115
Prognostic accuracy of magnetic resonance spectroscopy (MRS) biomarkers in neonates with hypoxic ischaemic encephalopathy (HIE): a systematic review and meta-analysis of diagnostics

CR RIZAVA[1], GN NIKOLAIDIS[2], CV VAS[1], PG GRIFFITHS[3], DC CONNOLLY[4], AH HART[5]
[1]Neonatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [2]Center of Health Economic, University of York, York, UK; [3]Academic Unit of Radiology, University of Sheffield, Royal Hallamshire Hospital, Sheffield, UK; [4]Paediatric Neuroradiology, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK; [5]Paediatric and Perinatal Neurology, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK

Objectives: Magnetic Resonance Spectroscopy (MRS) biomarkers have been used for prognostication of neurodevelopmental outcomes in newborns affected by HIE. Previous meta-analyses evaluated their prognostic properties primarily in non-cooled infants. Here, we also included recent studies on infants who received therapeutic hypothermia (TH), and meta-analysed the full evidence base to obtain updated predictive accuracy estimates.
Methods: We systematically searched MEDLINE, COCHRANE, EMBASE and CINHAL for studies assessing MRS for prognostication of adverse neurodevelopmental outcome (assessed ≥12 months) or death in infants (≥36 weeks gestation) affected by HIE. Data were extracted from eligible studies and meta-analysed using a bivariate approach in RStudio. Also, we assessed the impact of effect modulators such as therapeutic hypothermia in a subgroup analysis. Finally, the methodological quality of the included studies was rated using the QUADAS-2 tool.
Results: We retrieved 72 eligible studies of which 25 reported outcomes on prognostic accuracy of MRS biomarkers; five were performed in infants who had received TH. The biomarker lactate to N-acetylacetate (lac/NAA) ratio, measured in the basal ganglia, had a pooled sensitivity of 90.2% (95% CI: 84.9–94.7%) and a pooled specificity of 90.1% (95% CI: 84.6–94.7%) in predicting neurodevelopmental outcomes. The pooled sensitivity and specificity of the remaining biomarkers (i.e. lac/cr -creatinine-, NAA/cr, and NAA/cho -choline-) ranged from 64.3% to 84.8% and 79.2% to 94.9%. respectively. Subgroup analysis revealed that sensitivity and specificity increased slightly in the cooled compared to the non-cooled group (mean sensitivity 91.3% vs 88.1%, mean specificity 91.5% vs 87.9% respectively).
Conclusion: Lac/NAA measured by MRS can accurately predict adverse neurodevelopmental outcomes in infants with HIE. Therefore, Lac/NAA may be a potential surrogate marker for studies evaluating new therapies for HIE.

Poster No. 116

The relationship between magnetic resonance spectroscopy (MRS) in perinatal hypoxic ischaemic encephalopathy (HIE) and developmental outcome

CR RIZAVA[1], EH HOYLES[2], JL LARSEN[2], KM MACKAY[1], CV VAS[1], PG GRIFFITHS[3], DC CONNOLLY[2], AH HART[4]

[1]Department of Neonatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [2]Department of Paediatric Neuroradiology, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK; [3]Academic Unit of Radiology, University of Sheffield, Royal Hallamshire Hospital, Sheffield, UK; [4]Department of Paediatric & Perinatal Neurology, Sheffield Children's Hospital NHS Foundation Trust, Sheffield, UK

Objectives: To examine how MRS from the deep grey matter (DGM) and parieto-occipital white matter (POWM) differ between acute profound and chronic partial forms of HIE, and to examine their ability to predict developmental outcome.
Methods: Retrospective case note review of 63 neonates with HIE who had MRS within 7 days of birth. MRI results were grouped into acute profound, chronic partial, normal or other abnormalities. Acute profound, normal and other abnormalities groups were combined as they represented a spectrum of acute profound HIE. Developmental outcome was obtained from clinical records. MRS values were compared between imaging and outcome groups.
Results: 31/63 (49.2%) had abnormal MRI: 4/31 (12.9%) acute profound, 19 (29.0%) chronic partial, and 18 (58.1%) other abnormalities. No differences in MRS from the DGM were seen between MRI groups. NAA was lower and lactate higher from the POWM in participants with chronic partial compared to acute profound HIE. The optimal markers for developmental outcome were NAA from the DGM (sensitivity 67%, specificity 90%) and NAA from the POWM (sensitivity 67%, specificity 90%).
Conclusions: MRS differs between the DGM and POWM depending on the pattern of brain injury. It is possible MRS may need to be measured from different parts of the brain to discriminate adverse motor and cognitive outcomes, or from different regions of the brain depending on the pattern of injury to maximise its predictive ability.

Poster No. 117

Evaluating a new coma/consciousness scale in healthy, term neonates

E MATTHEWS[1], L CUTSEY[2], D EVANS[3], J GOODDEN[4], AR HART[1]

[1]Department of Perinatal Neurology, Sheffield Children's NHS Foundation Trust, Ryegate Children's Centre, Sheffield, UK; [2]Department of Paediatric Neurology, Leeds General Infirmary, Leeds, UK; [3]Yorkshire Neonatal Network, Wakefield, UK; [4]Department of Paediatric Neurosurgery, Leeds General Infirmary, Leeds, UK

Objective: To investigate whether a novel Neonatal Coma Score (NCS) produced consistent 'normal' scores in healthy, term neonates, and to investigate inter-observer reliability of the NCS.
Method: A new coma score (NCS) was designed by a Paediatric Neurologist, Paediatric Neurology Nurse, Neonatal Nurse, and Consultant Paediatric Neurosurgeon based on the Glasgow Coma Score that was developmentally appropriate for newborn babies. The NCS is a 15-point score with the following subsections of scoring: Best Motor Response (BMR), Best Verbal/Alertness Response (BVAR), and Best Eye Opening Response (BER). We prospectively recruited 100 healthy neonates from Jessop Wing Hospital, Sheffield, from the newborn physical examination clinic. Babies were scored by a midwife and researcher. Inter-observer correlation scores were calculated using an intra-class correlation coefficient (ICC).
Results: The median score for both the researcher and midwives was a total score of 15/15. The subsection median scores were: 6/6 for BMR, 5/5 for BVAR, and 4/4 for BER. The researcher scored 98% of neonates 13 or more in total, and the midwives scores 94% 13 or more out of 15. The ICC was in the 'Excellent' level of agreement range for the total NCS score (ICC=0.779, 95% confidence interval 0.671–0.851). The ICC values for the subsections of the score had 'Good' levels of agreement (ICC BMR=0.667, BVAR=0.701, BER=0.690).
Conclusions: This pilot study has shown a 'normal' NCS score for a neonate is 13 or more, and the NCS has high inter-rater reliability. Further research is needed on use of the NCS in unwell/premature neonates.

Poster No. 118

Are parental views of their child's development as accurate as formal developmental screening tools? A pilot study

E MCNAMARA[1], A FADILAH[3], K MACKAY[2], AR HART[3]

[1]University of Sheffield Medical School, Sheffield, UK; [2]Department of Neonatology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [3]Department of Perinatal and Paediatric Neurology, Sheffield Children's NHS Foundation Trust, Sheffield, UK

Background: Children at high risk of developmental difficulties are enrolled in developmental follow-up schemes, which may involve a standardised developmental screening tool. There is little published data on which tool is the most effective or whether asking the parents if their child's development is normal or not is as effective.

Objectives: To review the ability of two simple parental questions designed to identify children with developmental difficulties compared to standardised developmental screening tools.
Methods: Children aged 22 to 36 months attending developmental follow-up clinics were invited to participate. Parents were asked: question 1 - whether their child's development was 'normal', 'abnormal' or 'don't know', and question 2 to grade their child's developmental abilities on a Likert Scale. Parents also completed the Ages and Stages Questionnaire 3rd Edition and the Parental Report of Children's Abilities Revised (PARCA-R). Their clinician performed a Schedule of Growing Skills (SOGS). A blinded assessor performed the Bayley Scales of Infant and Toddler Development 3rd Edition (BSID3). Abnormal development was defined as either: a BSID3 composite score <70 or <80. Sensitivities and specificities were calculated. The abilities of the screening tests were compared using McNemar test; $p<0.05$ was assumed statistically significant.
Results: 34 children were recruited. 22 completed PARCA-R. Parental question 1 had sensitivity 85.7%, specificity 42.1% for BSID3 <70; sensitivity 80.0%, specificity 46.2% for BSID<80. Statistically significant differences were found between question 1 and the other screening tests. Parental question 2 had sensitivity 92.9%, specificity of 68.5% for BSID3<70; sensitivity 80.0%, specificity 76.9% for BSID3<80. PARCA-R had significantly better diagnostic abilities than parental question 2. No significant

differences were found between the diagnostic abilities of the standardised tests.
Conclusions: Simple questions asking parents to identity whether their child's development is normal are poor diagnostic tools. Larger studies are needed to compare the effectiveness of standardised developmental screening tools.

Poster No. 119
Kernicterus in infants from ethnic minority groups in North East England

D BASKARAN[1], J RAPER[1], D MITRA[2], AP BASU[1,3], KK PANG[1]
[1]*Paediatric Neurology, Great North Children's Hospital, Newcastle upon Tyne, UK;* [2]*Neuroradiology, Royal Victoria Infirmary, Newcastle upon Tyne, UK;* [3]*Population Health Sciences Institute, Newcastle University, Newcastle upon Tyne, UK*

Objective: UK cases of kernicterus have been recorded in the 2003 to 2005 British Paediatric Surveillance Unit (BPSU) study and the National Neonatal Research Database (NNRD). BPSU identified 14 over 2 years and NNRD had 2 to 8 per year in 2012 to 2015. We were aware of recent cases in our North East region and therefore reviewed our cohort at Great North Children's Hospital, Newcastle upon Tyne, UK.
Methods: Retrospective notes review of children diagnosed with kernicterus between January 2005 and June 2020, recorded in our paediatric neurology database.
Results: Three infants were identified, all born in UK after December 2017. All were term weighing 3.2 to 3.8kg. Ethnicities were Asian, African and Arabic. All had midwifery review within 72 hours of birth. Maximum bilirubin levels were 483mmol/L (day 8), 615mmol/L (day 5) and not recorded in one. Two had phototherapy and none had exchange transfusion (recommended when >450mmol/L, NICE CG98). One presented at 5 days with apnoea, encephalopathy and cardiovascular compromise. The others were only diagnosed at 5 and 7 months, following investigations for developmental delay. MRI revealed bilateral increased T2 signal in globus pallidus in all cases. One had additional bilateral restricted diffusion in mesial temporal structures. One had Glucose 6-Phosphate Dehydrogenase deficiency whereas the others had no identified underlying pathology. Two have significant dystonia and one has bilateral sensorineural hearing loss.
Conclusions: We had three cases of kernicterus in 2.5 years which is unexpectedly high, and existing national numbers may be underestimates because late presentations as noted by us may not get recorded in NNRD. All were from non-white backgrounds in whom visual assessment of jaundice can be affected by skin tone. With changes in UK ethnic population, revision of local guidelines to include more objective measures like transcutaneous bilirubinometry is needed.

Poster No. 120
Double trouble – A case of congenital myotonic dystrophy and hypoxic ischaemic encephalopathy

M PARMAR[1], Z MUDASIRU[1], G AMBEGAONKAR[2], N MERCHANT[1]
[1]*Neonatology, West Hertfordshire Hospitals NHS Trust, Watford, UK;* [2]*Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK*

Background: Hypoxic ischaemic encephalopathy (HIE) is defined as an acute brain dysfunction following lack of cerebral blood flow and oxygen delivery. The term 'neonatal encephalopathy' (NE) is preferred as there are other possible aetiologies. We present a case of Congenital Myotonic Dystrophy (CMD) and HIE and review current literature about co-existence of these conditions.
Case history: A term, 3.5kg, female infant of non-consanguineous parents required unexpected cardio-pulmonary resuscitation following an elective caesarean section for breech presentation. Cord gases were normal. Polyhydramnios was noted in the third trimester with otherwise normal antenatal scans and serology. Hypotonia, ineffective suck and incomplete Moro reflex was noted with macrocephaly, widened skull sutures and upper limb contractures. aEEG was moderate suppressed. Day 7 MRI showed reduced cortical folding, ventriculomegaly, focal lesions in white matter & lentiform nucleus with no myelination in the posterior limb of internal capsule. Hypotonia persisted post cooling so further investigations were sent, with genetics confirming CMD.
Discussion: CMD is a common neonatal genetic neuromuscular disorder, caused by an unstable cytosine-thymine-guanine trinucleotide repeat in the myotonic dystrophy protein kinase (DMPK) gene. Review of literature for CMD and neonatal encephalopathy co-existing was sparse with one cohort study of 9 CMD patients and 3 case reports, all showing white matter injury and clinical encephalopathy in newborns with CMD with absence of the features suggestive of HIE as per American College of Obstetricians and Gynecologists Task force of Neonatal Encephalopathy criteria.
Conclusion: As the clinical presentation of CMD may mimic HIE, and especially if the neuroimaging is atypical for this, there should be a high index of suspicion for investigating other causes of HIE. We suspect that CMD causes increased vulnerability of the white matter to secondary hypoxic ischaemic changes.

Poster No. 121
Current evidence for the treatment of hereditary spastic paraplegia with intrathecal baclofen or selective dorsal rhizotomy

HM ROBERTSON[2], DE LUMSDEN[1]
[1]*Complex Motor Disorder Service, Evelina London Children's Hospital, London, UK;* [2]*Royal Free Hospital, London, UK*

Objective: Hereditary spastic paraplegia (HSP) is a heterogeneous group of genetic disorders characterised by progressive weakness and spasticity of the lower limbs. Treatment is supportive, targeting reduction in spasticity to improve comfort and function. We sought to review the current evidence for intrathecal baclofen (ITB) or selective dorsal rhizotomy (SDR) in HSP.
Method: A systematic review was performed using the NICE HDAS service; the search strategy returned results matching

hereditary spastic paraplegia or genetic spasticity with either intrathecal baclofen or selective dorsal rhizotomy.
Results: 12 results for the use of ITB and 4 for SDR met the inclusion criteria. Reported outcome measures included subjective reporting of patient symptoms and objective measures including the modified Ashworth scale (MAS) (11), GMFCS (3), GMFM (2), electrophysiological recordings of gait (6) and urodynamic function (1). 48 patients treated with ITB were identified. The mean MAS improvement by last follow-up was 1.78 (95% CI 1.49–2.08). There were 12 reported complications, relating to catheter displacement, malfunction or infection. 12 patients were identified that underwent SDR. The typical extent of rhizotomy was L2 – S1 with mean 54% rootlets cut. The mean MAS improvement by last follow-up was 1.75 (95% CI 1.27–2.24). There were 4 reported complications including postoperative paraplegia, severe dystonia and two episodes of increased frequency of falls. There was no evidence to suggest that either treatment was superior in reducing MAS (p=0.899).
Conclusion: Evidence for the use of ITB or SDR in HSP remains limited. ITB is a reversible treatment with the opportunity to titrate dose delivery to clinical effect. SDR is an irreversible treatment, but may be definitive. Complications are reported frequently in both. Reports to date suggest improvement in spasticity and function may be possible following either treatment.

Poster No. 122
Peak width of skeletonised DTI Metrics as a marker for white matter disruption in dyskinetic cerebral palsy

DE LUMSDEN[1], J ASHMORE[2], G CHARLES-EDWARDS[2], JP LIN[1]
[1]Complex Motor Disorder Service, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Medical Physics, St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK

Objective: Peak Width of Skeletonised Mean Diffusivity (PSMD) is a fully automated, MRI biomarker which provides a quantitative measure of diffuse white matter injury. We aimed to explore the utility of PSMD in a cohort of children with Dyskinetic Cerebral Palsy (DCP).
Methods: Diffusion Tensor Imaging (DTI) was acquired at 1.5 Tesla in 30 children with DCP, split into more functional (GMFCS level I–III, n=8), and less functional (GMFCS levels IV–V, n=22) groups. PSMD was measured and compared between these two groups, along with a modification of this automated approach to measure Peak Width of skeletonised Fractional Anisotropy (PSFA), and mean skeletonised FA and MD.
Results: Both PSMD and Mean MD where greater in the less functional group (Mann-Whitney U-test, $p<0.05$). Mean FA, but not PSFA was significantly lower in the less functional group. Taken collectively, these results are suggestive of widespread white matter disruption in the more severely impaired children.
Conclusion: PSMD, and modifications of this technique extracting metrics from skeletonised white matter, provide potential quantitative biomarkers to explore white matter disruption in children with neurological disorders. These techniques have low computational requirements, and can be automatically implemented. Higher PMSD, higher mean MD, and lower mean FA in children with more severe DCP supports a widespread white matter abnormality as a potential pathophysiological contributor in DCP.

Poster No. 123
Movement disorder manifestations of ataxia-telangiectasia: a systematic review

E PETLEY[1], S OJHA[1,2], WP WHITEHOUSE[1,3]
[1]School of Medicine, University of Nottingham, Nottingham, UK; [2]Children's Hospital, University Hospitals of Derby and Burton, Derby, UK; [3]Paediatric Neurology, Nottingham Children's Hospital, Nottingham University Hospitals NHS Trust, Nottingham, UK

Objectives: To document the movement disorder manifestations of Ataxia-Telangiectasia (A-T)
Methods: 17 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 A-T within the article, not an original article, animal studies, article not clinically relevant.
Results: Search returned 194,890 articles; 14,622 titles and abstracts were reviewed after removing 180,268 duplicates. Full text review of 1,163 articles was performed and 1,039 studies were included (13,459 exclusions, 124 excluded after full text review). Ataxia was reported in 2840 cases (367 studies) at a median age of onset (n=353) of 2 years 0 months (interquartile range 1 year 3 months–4 years 0 months). Also 1,338 movement disorders were reported in at least 851 cases. The most common movement disorder reported was choreoathetosis with 301 cases (55 studies) at a median age of onset (n=20) of 12 years 6 months (interquartile range 4 years 0 months–24 years 0 months). Tremor was the second most common movement disorder reported with 298 cases (70 studies) at a median age (n=26) of 12 years 0 months (IQR 8 years 0 months–19 years 9 months). Other movement disorders reported in the literature included dystonia, myoclonus, unspecified hyperkinesia, and unspecified bradykinesia. Specific variant and classical A-T data has been analysed and will be presented.
Conclusions: This study is the first comprehensive systematic review of scientific literature on this topic. This completed review has informed the current Natural History of A-T (N-HAT) study, a retrospective, longitudinal and cross–sectional study.

Poster No. 124
Deep brain stimulation evoked potentials in children with dystonia

VM MCCLELLAND[2,3], A VALENTIN[2], E FODDAI[2], T DENISON[1], JP LIN[3]
[1]Institute of Biomedical Engineering, University of Oxford, Oxford, UK; [2]Basic and Clinical Neuroscience, IOPPN, King's College London, UK; [3]Children's Neurosciences, Evelina London Children's Hospital, Guys and St Thomas' NHS Foundation Trust, London, UK

Objectives: Pallidal Deep Brain Stimulation (DBS) is an established therapy for dystonia. Stimulation parameters, including selection of active electrode contacts, are currently determined empirically. Recording the cortical response to the pallidal stimulus, known as Deep Brain Stimulation Evoked Potentials (DBSEPs) could provide a more objective measure of optimal contact selection.

Methods: Fifteen young people (age 7–19 years, mean 13.71) with dystonia participated, all with bilateral pallidal DBS implanted at least 6 months previously. Scalp EEG was recorded via an ASA (ANT-Neuro) system, using 10-20 international electrode placement and impedances <10kOhm. Data were sampled at 5KHz. Contacts from each stimulating electrode were tested separately, using 6Hz bipolar stimulation, with the other side turned off. Pairs of electrode contacts were tested sequentially using combinations of cathodal stimulation with an adjacent anode. Voltage was 2V, with pulse width maintained at the patient's therapeutic level. Each combination was recorded for 3 minutes, giving >1000 stimuli per contact pair. Therapeutic settings were restored on study completion. Offline, the DBS stimulus artefact was used to segment EEG data into epochs (10ms pre-stimulus, 150ms post-stimulus). Portions of data contaminated by movement/muscle artefact were excluded. Remaining epochs (900–1100 per patient after removing artefacts) were averaged to obtain the DBSEP for each contact pair. Onset and peak latencies and peak amplitudes were recorded.
Results: Clear DBSEPs were obtained in 12/15 patients on one or both sides, with peak latency of 20ms, and largest amplitude over the ipsilateral central/centro-parietal region. Both the peak latency and topography were in keeping with adult literature. In 3/15 patients no convincing DBSEP was obtained.
Conclusion: This study confirms the feasibility and tolerability of this challenging technique in children with DBS for dystonia. Future work will investigate the potential clinical application of DBSEPs to inform an objective and individualised approach to DBS contact and parameter selection.

Poster No. 125
Inter-relation between hand functioning, cognition and quality of life of CP children: prospective randomized study

VK KOZYAVKIN, TV VOLOSHYN
International Clinic of Rehabilitation, Truskavets, Ukraine

Objective: Multidisciplinary approach is often promoted but it is not cost-efficient to involve all medical staff and use wide variety of diagnostic and intervention tools for every single patient.
Background: Having knowledge on pivotal manifestations of CP and what are they related to would ease implementation of multidirectional approach in practice. It will shorten a search of pathologies only to those related to main manifestations of the disease and allow to treat main symptoms related to quality of life.
Methods: 612 children aged 2 to 18 years (mean age 6y 5mo) with CP (G.80): examined by 3 independent doctors. 56% males, 44% females. Randomized blinded assessment. Fine hand function assessed by "9-hole peg" test, "Box and Blocks" test, dynamometry. Intellectual functioning assessment was done using Raven Matrices. Quality of Life (QoL) assessment according to Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD). The intraclass correlation coefficient (ICC) was used for finding out discrepancies between observers. Inferential statistics including 95% CI and *p*-value. Spearman's rank correlation coefficient for non-parametric measures of variables.
Results: ICC coefficient between observers was reliable–0.93 (95% CI: 0.89–0.95). The mean QoL score for children GMFCS levels I and II was 58.4 (SD 16.5), for GMFCS III, IV and V children–22.2 (SD13.4). QoL was more related to fine hand functioning (r=0.344) than to cognition (r=0.292). There was a strong correlation bond between fine hand functioning and cognition (r=0.663). In case fine hand function improved positive changes in cognition were observed in 74% of participants ($p<0.05$). Correlation between grasp power and IQ was weak (r=0.185). Also grasp power improvement was slightly related to QoL (r=0.102).
Conclusion: Most important part of the research was the benefit from finding out bond between cognition, hand functioning and quality of life. The quality of life is the most important of all and our final aim is QoL improvement to the highest extent possible. Study allowed to understand what is better to work on (hand accuracy but not power) for improvement of cognitive functioning. Positive changes in fine hand functioning improve QoL even more that cognitive changes. So training of fine motor skills should be given a priority in case of limited rehabilitation resources.

Poster No. 126
The changing face of reported status dystonicus

DE LUMSDEN[1], NM ALLEN[2]
[1]Complex Motor Disorder Service, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK; [2]Department of Paediatrics, National University of Ireland, Galway, Ireland

Objectives: Status Dystonicus (SD) represents the most severe end of the spectrum of dystonia. We aimed to review reported cases of SD to date, exploring whether presenting features, management and outcomes have changed over time.
Methods: Firstly, data was extracted from two previous case series, presenting reported cases up until 2012 and from 2012 to 2017 respectively. Secondly, and updated literature review was performed, identifying reported cases of SD since 2017. Extracted data included age at SD episode, trigger for SD, use of neurosurgical interventions, and outcome following SD.
Results: A total of 187 episodes in 160 patients were identified (89 episodes in 68 patients up until 2012, 44 episodes in 41 patients 2012–2017, and 54 episodes in 51 patients from 2017–2020). In all three epochs, the majority of episodes were reported in children (58.8%, 79.9% and 85.2% respectively), with no trigger for SD identified in a significant minority of cases (32.6%, 28.0% and 37.4% respectively). In each epoch, the commonest trigger was infection/inflammation. Medication change-related SD decreased in frequency, whilst Deep Brain Stimulation-related SD increased over time. Neurosurgical interventions were more frequently reported in later epochs (40.0%, 65.9% and 66.7% respectively). Return to/improvement compared to baseline was reported in 73.4%, 70.5% and 64.8% of SD episodes respectively. Reported mortality was 1.9% in the final epoch, compared to 10.3% and 11.6%. No prospective epidemiological studies of SD were identified.
Conclusions: Over time, SD remained most commonly reported in children, with a trigger for SD identified in around two-thirds of episodes. Reports of medication change-induced SD have become less frequent, whilst episodes of DBS related SD have become more frequent. Neurosurgical interventions are now reported in the majority of cases of SD. Overall outcomes from SD remain largely unchanged over time, though reported mortality appears to have declined.

Poster No. 127

An infant with unusual unilateral movements

A PARIDA[1,2], A SUDARSANAM[1], H COX[3], R GUPTA[1]
[1]Department of Paediatric Neurology, Birmingham Children's Hospital, Birmingham, UK; [2]Department of Paediatric Neurology, Oxford Children's Hospital, Oxford, UK; [3]Department of Clinical Genetics, Birmingham Women's Hospital, Birmingham, UK

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 128

Predictability of GMA (Prechtles manoeuvre) in assessment of cerebral palsy—trial on high risk neonate at child development centre, semi urban area

N MUKHERJEE
IAP, Mumbai, India

Objective: To segregate the high risk newborn and follow up properly. To implement General Movement Assessment on them. Early diagnose possibility of cerebral palsy and arrest it at stage of evolution.
Method: We made a team (all trained on GMA), contacted SNCU of nearby Govt medical College to allow us to visit the kids at the routine follow-up clinic. The study took place for 1 year (July18–June19). We started with both term and preterm neonate not before 34 weeks of gestational age. With the baby positioned supine, movements are video-recorded and analysed by us to categorise the movements according to their fluency, complexity and variability. Two specific abnormal GM patterns reliably predict later cerebral palsy: (1) a persistent pattern of cramped-synchronized GMs. The movements appear rigid and lack the normal smooth and fluent character. Limb and trunk muscles contract and relax almost simultaneously. (2) The absence of GMs of fidgety character. So-called fidgety movements are small movements of moderate speed with variable acceleration of neck, trunk, and limbs in all directions. A total number of 67 children were enlisted for the study, selected according to high risk category, of which 12 guardians did not turn up for regular visits and defaulted. 5 parents were noncompliant. All the children taken in first 3 months (n=50) were observed twice, 6 and 9 months of age (corrected age in case of preterm).
Results: It came to our notice that among this 50 number of children history wise 26 from birth asphyxia with variable HIE I&II, 6 from kernicterus encephalopathy, 16 preterm low-birth weight, 2 with early onset seizure. Among these, 34 children demonstrated typical movement pattern at the 1st observation and 31 of them destined to be CP at 6 to 9 months of age.
Conclusion: Beside a sensitivity and specificity of 95% each, the assessment of GMA is quick, non-invasive, even nonintrusive, and cost-effective compared with other techniques.

Poster No. 129

A teenager with a complex movement disorder

MR SMITH[1,2], S RAMDAS[1,2], D SHEARS[1,2], AH NEMETH[1,2]
[1]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]University of Oxford, Oxford, UK

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 130

Homozygous frameshift variants in PDE10A; another founder neurological disorder found amongst the Roma

CE REYNOLDS[3], B LYNCH[2], SA LYNCH[1], KM GORMAN[2]
[1]Clinical Genetics, CHI at Temple Street, Dublin, Ireland; [2]Paediatric Neurology, CHI at Temple Street, Dublin, Ireland; [3]Paediatrics, CHI at Crumlin, Dublin, Ireland

Objective: To describe a case of a hyperkinetic movement disorder due to homozygous variant in PDE10A.
Case report: A 13 year old female born to consanguineous Polish-Roma parents presented aged 1 year with dystonia, developmental delay, failure to thrive and hypotonia. Dystonic movements began aged 2 months. Over the following 12 years, she developed a mixed hyperkinetic movement disorder characterised by choreoathetosis, dyskinesia and dystonia affecting her head, neck, trunk and limbs. She had dysarthric speech and mobilised by wheelchair. She achieved average scores on cognitive testing. Extensive metabolic, radiological and genetic investigations were normal. Whole-exome sequencing identified a homozygous PDE10A frameshift variant (c.607del: p.IIe203fs). The mother was heterozygous for the variant. Father is not available for testing. This exact variant has not been reported previously. A trial of levodopa was commenced after the genetic diagnosis with *Objective:* improvement in movements, with less choreiform and dyskinetic movements of her upper limbs enabling a functional improvement of fine motor tasks.
Discussion: PDE10A encodes phosphodiesterase 10A, which regulates the degradation of cAMP and cGMP in medium spiny neurons of the corpus striatum. Both homozygous and dominant variants in PDE10A lead to a loss of enzymatic function and are associated with childhood-onset chorea. Homozygous variants display a more severe phenotype, characterised by delayed motor and language milestones, central hypotonia, early-onset chorea, severe dysarthria, and occasionally mild intellectual disability. MRI brain imaging is normal in homozygous variants but abnormal in heterozygous variants with symmetrical T2-hyperintense striatal lesions. To date, homozygous variants have only been reported in ten individuals from three consanguineous families. Our patient is the first reported individual from the Polish Roma population.

Poster No. 131

Genetic diagnostic rates in paediatric ataxia

KL GARRARD[2], KE ALLEN[2], S CAMPBELL[2], N BEAUCHAMP[1], M PANAYI[1], S MORDEKAR[1]

[1]Sheffield Children's NHS Foundation Trust, Sheffield, UK; [2]Sheffield Hallam University, Sheffield, UK

Aims: Next generation sequencing (NGS) has increased the number of genes which can be reasonably examined per patient. This service review aims to determine the diagnostic rate of genetic testing for referrals for paediatric ataxia.

Methods: The Sheffield Diagnostic Genetics Service (SDGS) NGS ataxia panel comprises 144 genes associated with ataxia. The episodic ataxia (EA) panel comprises 11 genes. Both include genes previously offered as single tests. Data for testing between 2010 and 2019 was analysed. Cases with pathogenic variants were assessed to check that variants were diagnostic. Where a variant of uncertain clinical significance was present or a single pathogenic variant in a recessive disorder, results were recorded as inconclusive. Diagnostic rates for single gene and NGS testing were compared.

Results: 704 ataxia patients were referred to SDGS for genetic testing: 166 EA single gene, 185 EA NGS panel, 219 ataxia single gene and 134 ataxia NGS. Genetic diagnoses were identified in 32 (19.3%) of single gene EA tests and 17 (9.2%) of EA NGS panels with inconclusive results in a further 8 (4.3%) of NGS tests. Genetic diagnoses were identified in 16 (7.3%) single gene ataxia tests and 32 (24%) of ataxia NGS with a further 28 (21%) NGS tests inconclusive.

Conclusions: NGS testing can significantly increase diagnostic rates when a clinical feature can have widely varying genetic causes (7.3% vs 24%). However, where panel testing is used on a broader pool of patients with a previously specific phenotype, positive diagnosis rates can appear to be reduced (19.3% vs 9.2%).

Poster No. 132

Oculogyric crisis and Parkinsonism with Risperidone: a case report

SI HONEYMAN[1,3], R TAILOR[1], S JAYAWANT[1], M SMITH[1], R SHEPPERD[2], S RAMDAS[1], G ANAND[1]

[1]Paediatric Neurology Department, John Radcliffe Hospital, Oxford, UK; [2]Oxford Health NHS Foundation Trust, Oxford, UK; [3] Department of Medical Sciences, University of Oxford, Oxford, UK

Oculogyric crisis (OGC) is an acute dystonic reaction, characterised by prolonged involuntary upward deviation of the eyes. This condition is known to be precipitated by typical antipsychotics, such as Haloperidol, but is rarely seen with atypical antipsychotics (e.g. Risperidone). Risperidone is being used increasingly for behavioural indications in children, although the side effect profile in this population remains poorly defined. We present only the third reported case of oculogyric crisis associated with Risperidone use in a paediatric patient. A 17-year-old boy was admitted to our institution with complaint of intermittent episodes of upward eye deviation, of duration 45-90 minutes, occurring over a 6-month period. The patient had a significant background of ADHD, autism, epilepsy and bipolar disorder, with regular medications including Risperidone 4mg OD, Aripiprazole 2mg OD and Sodium Valproate (400mg OM/700mg ON). In addition to episodes of gaze elevation, the patient demonstrated signs of Parkinsonism. On examination the patient was hypomimic, with slowed speech and drooling. There was a paucity of movement, difficulty initiating actions, shuffling gait, reduced arm swing and intermittent bilateral resting tremor. The patient was managed with gradual weaning off Risperidone. Upon cessation of the medication, no further episodes were reported, and Parkinsonian symptoms regressed. Risperidone acts through 5-HT2 and D2 receptor antagonism. Compared to atypical anti-psychotics, it has been thought to have a relatively safe side effect profile, with extra-pyramidal symptoms almost exclusively associated with doses over 6mg/day. However, it has been suggested the paediatric population may be more susceptible to anti-dopaminergic effects of Risperidone; in vivo models demonstrated more significant upregulation of forebrain DA receptors in juvenile animals compared with adults, and case series report higher incidence of extra-pyramidal effects in paediatric populations. This case should raise awareness for the potential presentation of OGC in association with Risperidone use in the adolescent population.

Poster No. 133

KMT2B related dystonia - adult onset and induced by inter-current illness?

LMC GREEN[1], H CLIFFE[2], HG MCCULLAGH[1]

[1]Department of Paediatric Neurology, Leeds Teaching Hospitals Trust, Leeds, UK; [2]Department of Radiology, Leeds Teaching Hospitals Trust, Leeds, UK

Objectives: Since 2016 KMT2B related dystonia has been reported in over 70 cases of childhood onset dystonia, the majority presenting in the first decade with a progressive dystonia. Bulbar involvement and communication difficulties are often reported and associated intellectual disability is common. Though the majority of cases are caused by de novo variants, around 15% are inherited from a parent. There is a high degree of inter-familial variability and 1/3 of parents are asymptomatic. Here we present a non-progressive case of KMT2B childhood onset dystonia whose father presented with dystonia aged 21 years following a diarrhoeal illness.

Case: Having been diagnosed with diplegia and microcephaly at a younger age, an Asian male was referred to the neurology team aged 13 years with "sticky legs". Examination revealed mild lower limb dystonia without spasticity and brisk DTRs throughout. Gait was normal and he was able to run without difficulty. There was no evidence of dysarthria and though he had some issues with handwriting and mild learning difficulties he attended mainstream school without support. His father presented acutely aged 21 years during a prolonged stay in India during which he suffered an acute diarrhoeal illness and significant weight loss. During his recovery phase he developed hemi-ballismic movements of the arm and changes to his voice which progressed for around 8 years before stabilising. For the last 30 years he has remained stable with left proximal upper arm dystonia and a fixed dysarthria. He feels his symptoms are partially helped by L-dopa and trihexyphenidyl.

Results: Extensive investigations were performed for both the father and son, including brain MRI which was unremarkable. Dystonia panel testing revealed a heterozygous KMT2B c.[4789C>T] mutation.

Conclusions: These cases further highlight the reduced penetrance and familial variability seen in KMT2B-associated dystonia,

specifically its presentation following acute illness and a relatively mild and non-progressive course.

Poster No. 134

Not another cause of intracranial calcification! CYP2U1 mutation resulting in complicated HSP phenotype with intracranial calcification

LMC GREEN[1], R SINGH[2], G VADLAMANI[1]
[1]Department of Paediatric Neurology, Leeds Teaching Hospitals Trust, Leeds, UK; [2]Department of Paediatrics, Mid Yorks Teaching Hospitals Trust, UK

Objectives: CYP2U1 mutations have been reported in families with complicated hereditary spastic paraplegia (HSP). There are high levels of intra- and inter-familial phenotypic variability, ranging from mild disability and difficulty running to a 4-limb motor disorder with intellectual impairment and regression with progressive encephalopathy, spasticity and dystonia. White matter abnormalities have previously been reported, predominantly delayed myelination, and 3 previous cases have demonstrated intracranial calcification.
Case: A female infant, the second child of non-consanguineous Caucasian parents, presented from infancy with global developmental delay. Other than mild blunt-force injury to the abdomen pregnancy was unremarkable and the neonatal period uneventful. She walked only with support and on her toes. Findings on examination were consistent with spastic diplegia in the form of hypertonia, brisk DTRs, ankle clonus and extensor plantars. She had significant intellectual impairment. Ophthalmology examination revealed a choroidal nevus in the right eye. Mobility declined from 12 years with increasing spasticity and the appearance of dystonia. She developed hip dislocation and lower limb contractures.
Results: Extensive investigation, including white cell enzymes, CSF neurotransmitters and CGH array were normal. Cranial MR aged 5 years was normal, but repeat aged 11 years demonstrated areas of high signal in the periventricular white matter. Aged 16 years repeat MR showed mineral deposition in the basal ganglia and mid brain, confirmed on CT as calcification. Whole exome sequencing revealed CYP2U1 mutation, confirming a diagnosis of hereditary spastic paraplegia 56.
Conclusions: In cases of HSP basal ganglia and periventricular calcifications on imaging should raise the possibility of CYP2U1.

Poster No. 135

MPPH Megaencephaly–Postaxial polydactyly–Polymicrogyria–Hydrocephalus syndrome

T KHAN[1], C DE GOEDE[1], R SINHA[1], J CAIN[1], S DOUZGOU[2]
[1]Royal Preston Hospital, Preston, UK; [2]St Mary's Hospital, Manchester, UK

Introduction: We present a case of MPPH. This condition has only recently been described and the phenotype is still evolving. This case showed the perisylvian polymicrogyria and ventriculomegaly on imaging. We will describe the clinical features and will share the imaging findings.
Case presentation: A male infant born in good condition at 39 weeks presented with macrocephaly and seizures at 1 week of age. He had significant developmental delay and visual impairment. We have serial repeat Magnetic Resonance imaging from 1 to 15 months which were not suggestive of hydrocephalus although ventricles remained enlarged bilaterally. His hypertonia and lax ligaments were characteristic of AKT3 gene mutation which he had. The radiological findings and the genetic test results confirmed MPPH syndrome.
Discussion: In MPPH AKT3, PIK3R2 or CCND2 genes mutations result in brain overgrowth causing disruption of the cerebral cortex resulting in developmental delay, feeding difficulties and seizures. Radiological features of MPPH can overlap with other disorders that cause megalocephaly such as Megalencephaly-Capillary Malformation Polymicrogyria syndrome (MCAP). Cortical malformations, especially perisylvian polymicrogyria and ventriculomegaly are the two most commonly described radiological findings in literature. The ventriculomegaly can be of a varying degree and approximately 50% of patients have frank hydrocephalus. In our patient, MR imaging demonstrates diffuse polymicrogyria predominating in the front parietal lobes and perisylvian regions bilaterally. Lateral ventricle enlargement with cavum septum pellucidum was evident in concordance with published case reports. A thick corpus callosum has also been described previously and is present in our case report. In addition to characteristic findings described in literature, imaging of our patient demonstrated focal T2 signal change and persistent diffusion changes in the superior cerebellar peduncles extending into the facial colliculi and medulla. This has not been described in literature; however the relevance of this finding remains indeterminate at present.

Poster No. 136

Utility of smart phone recording in a resource poor setting

EN UMEADI[1,3], WC IGWE[1,3], TS ECHENDU[1], AO ODITA[1,3], CU UFOAROH[2,4]
[1]Department of Paediatrics, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria; [2]Department of Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria; [3]Department of Paediatrics, Nnamdi Azikiwe University, Awka, Nigeria; [4]Department of Medicine, Nnamdi Azikiwe University, Awka, Nigeria

Objective: Parasomnias are a group of benign sleep disorders that are characterized by abnormal and unpleasant motor, verbal or behavioural events that occur during sleep or wake to sleep transitions. The objective of this report is to point out the challenges in the diagnosis of parasomnias in a resource-poor setting where diagnostic sleep studies are not available. Also, parasomnias must be excluded in suspected cases of seizures that have failed to respond to appropriate anti-seizure medications.
Method: We report two cases of parasomnias misdiagnosed as seizure disorders seen at Outpatient Paediatric neurology clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi, South-East Nigeria.
Results: Case 1 – A 13-year-old female presented to our facility with abnormal jerking movements, thrashing of the limbs and occasionally talking while sleeping of about 1-year duration. During episodes, she is unresponsive to calls or painful stimulus. An initial diagnosis of a seizure disorder was made. An electroencephalogram done was suggestive of a focal seizure. The patient was placed on appropriate anticonvulsant medications but responded poorly. Home video recording during sleep was requested and which confirmed the diagnosis of parasomnia. Case

2 – A 3-year-old female who presented with abnormal behaviour during night-time sleep described as high-pitched cry accompanied by blank stares and occasional hand movements. An electroencephalogram was not done due to financial constraints. The patient responded poorly to conventional anti-seizure medications. A smartphone home video recording obtained during sleep was suggestive of a diagnosis of parasomnia.
Conclusion: Parasomnias must be excluded in suspected cases of seizures that have responded poorly to appropriate anticonvulsants. A high index of suspicion, detailed sleep history, smartphone video recording of sleep events and sleep diaries are important in the diagnosis of parasomnias in resource-poor setting.

Poster No. 137

Dopamine transporter deficiency syndrome from infancy to adulthood: a new international cohort

J NG[1,2], JP LIN[3], E MEYER[2], JS MOHAMMAD[4,5,6], NC ØIEN[7], D HORN [8], MR SCHWEIGER[9], B DORAY[10], AS LEBRE[11], L CHRISTA[12], I DENZLER[13], J MUNTADAS[13], J ARMSTRONG[14], A GARCIA-CAZORLA[14], R ARTUCH[14], MA ALMUHAIZEA[15], H SAMPAIO[5], B TEHREEM[16], J KORNITZER[16], AA MATHEW[17], A DHERAI[18], SR MORDEKAR[19], E DAVIES[19], K BARWICK[2], D STEEL[2], AN DUTTA[20], M ALSWAT[21,22], O ALGHAMDI[21,22], S ALAMEER[21,22,23], NM ALSHAIKH[21,22,23], C SPAGNIOLI[24], C FUSCO[24], S POPE[25], SJR HEALES[25,27], MA KURIAN[2,26]
[1]Gene Transfer Technology Group, EGA Institute for Women's Health, University College, London, UK; [2]Developmental Neurosciences Programme, Great Ormond Street Institute of Child Health, University College London UK; [3]Department of Paediatric Neurology, Evelina Children's Hospital NHS Foundation Trust, London, UK; [4]Kids Neuroscience Centre, The Kids Research Institute, Children's Hospital at Westmead, University of Sydney, Australia; [5]TY Nelson Department of Neurology and Neurosurgery, the Children's Hospital at Westmead, Sydney, Australia; [6]Faculty of Medicine, The Children's Hospital at Westmead Clinical School, University of Sydney, Australia; [7]NeuroCure Clinical Research Center NCRC, Berlin, Germany; [8]Institute of Medical Genetics and Human Genetics, Charite, University Medicine Berlin, Germany; [9]Institute for Translational Epigenomics, Centre for Molecular Medicine, Cologne, Germany; [10]Department of Genetics, CHU La Reunion, Hôpital Félix Guyon, Saint Denis, Reunion; [11]Genetic and Biological Department, Reims University, Maison Blanche Hospital, Reims, France; [12]Metabolomic and Proteomic Biochemical Department, Necker Enfants-Malades Hospital, Paris Descartes University, Paris, France; [13]Department of Neurometabolic Diseases, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; [14]Institut de Recerca Sant Joan de Déu and Hospital Sant Joan de Déu, Barcelona, Spain; [15]Department of Neurosciences, AlFaisal University, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; [16]Department of Neurology, Rutgers New Jersey Medical School, New York, USA; [17]Department of Paediatric Neurology, Sagar Hospitals and Bangalore Baptist Hospital, Bangalore, India; [18]Department of Biochemistry, P.D.Hinduja National Hospital, Mumbai, India; [19]Department of Neurology, Sheffield Children's Hospital, Sheffield, UK; [20]Paediatric Neurology and Developmental Medicine Department, University of Basel Children's Hospital, Basel, Switzerland; [21]King Saud bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia; [22]King Abdullah International Medical Research Centre, Jeddah, Saudi Arabia; [23]Department of Paediatrics, Ministry of the National Guard - Health Affairs, Jeddah, Saudi Arabia; [24]Department of Paediatrics, Child Neurology Unit, AUSL-IRCCS di Reggio Emilia, Italy; [25]Neurometabolic Unit, National Hospital of Neurology and Neurosurgery, UK; [26]Department of Neurology, Great Ormond Street Hospital, London, UK; [27]Chemical Pathology, Great Ormond Street Hospital NHS Foundation Trust, UK

Objectives: Dopamine transporter deficiency syndrome (DTDS) is a rare monogenic neurotransmitter disorder. Classical presentation is with infantile parkinsonism-dystonia and caused by biallelic loss of function mutations in the SLC6A3 gene. We present a new DTDS cohort identified internationally between 2015-2020.
Methods: Patients were recruited through referral to Great Ormond Street UCL-Institute of Child Health or through international network of paediatric neurologists. Molecular diagnosis was confirmed through Sanger sequencing, gene panel and whole exome studies.
Results: 20 new classical DTDS patients were identified, median age of diagnosis 2.1 years (range 8 months–27 years). All presented with motor delay associated with dystonia (80%), axial hypotonia (65%), irritability (65%). All developed features of parkinsonism-dystonia with rigidity by 3 years. The children over 4 years (n=9, age 4–27 years) reported predominant bradykinetic movement disorder. 45% had eye movement disorder and all have bulbar dysfunction. Only 1 patient is verbal with single words, and the remainder are non-verbal. 11 patients had CSF neurotransmitters with 10 showing characteristic raised HVA:HIAA ratio. One child had normal ratio (2.9) with both metabolites raised. 18 children had MRI of which 1 was abnormal showing increased extra-axial space. None responded to pharmacological treatments. One child was misdiagnosed with cerebral palsy resulting in delayed diagnosis and 3 children died aged 3.6 and 10 years. Homozygous or compound heterozygous SLC6A3 mutations were identified including: deletion (1), frameshift insertion (1), intronic (1), nonsense (1), missense variants (12) of which 10 are previously unreported variants.
Conclusions: We present the largest single cohort of DTDS patients reported to date, with characteristic pharmacoresistant progressive infantile parkinsonism-dystonia. DTDS remains underrecognised with delayed diagnosis and should be considered in children presenting with progressive disorders of dystonia-parkinsonism, that may have been mis-labelled as CP.

Poster No. 137a

Abnormal dynamic neuronal connectivity in children with dystonia

DF SAKELLARIOU[2], S DALL'ORSO[1], E BURDET[1], JP LIN[3], MP RICHARDSON[2], VM MCCLELLAND[2,3]
[1]Biomedical Engineering and Human Robotics, Imperial College London, London, UK [2]Basic and Clinical Neuroscience, IOPPN, King's College London, London, UK [3]Children's Neurosciences, Evelina London Children's Hospital, Guys and St Thomas' NHS Foundation Trust, London, UK

Objectives: Dystonia is a network disorder resulting from dysfunction of, or abnormal connectivity between, sites within the cortico-basal ganglia-cerebellar network. Despite the dynamic nature of the disorder, stimulus-related changes in connectivity have not been studied. We investigate modulation of functional connectivity by a proprioceptive stimulus in young people with dystonia.
Methods: Sixteen young people with dystonia and eight controls (age 6–20 years, mean 12.5 years) participated. A robotic wrist interface delivered passive wrist extension movements of the right upper limb, producing a brief stretch of the wrist flexors (10 degrees from neutral). Scalp EEG was recorded using the 10-20 international system, with impedances below 10kOhm. EEG was amplified, filtered (DC-500Hz) and sampled at 2500Hz. Wrist position was monitored and movement onset was synchronised with EEG recordings. Data were segmented into 4.5 second epochs (1 second pre- and 3.5 seconds post-stimulus). Up to 160 epochs were averaged to produce a Stretch Evoked Potential

(StrEP) in each individual. Event-related network dynamics were estimated using the imaginary part of Wavelet Transform Coherency (WTC), excluding volume conduction. Bootstrapping was applied to test for significance against random coupling between brain areas. Global microscale connectivity (GMC) was calculated to estimate the overall engagement of areas into short-lived networks related to the StrEP. Global connectedness (GC) was calculated to estimate the spatial extent of the StrEP networks.
Results: Clear StrEPs were evoked over contralateral sensorimotor cortex. Individual dynamic connectivity maps revealed a striking difference between dystonia and controls, with particularly strong event-related connectivity in the theta (4–8Hz) band in dystonia. At group level, theta band GMC was significantly higher in dystonia than controls (p=0.045). GC was also stronger in dystonia than controls (non-significant trend).
*Conclusion:*Young people with dystonia show an exaggerated dynamic network response to proprioceptive stimuli, displaying excessive, widespread theta-band synchronisation and over-recruitment across the sensorimotor network.

Poster No. 138
Prediction of thalamic dysfunction by sleep spindles in children with migraine

E ULGEN TEMEL, P OZBUDAK, E ARHAN
Pediatric Neurology, Gazi University Faculty of Medicine, Ankara, Turkey

Introduction: Migraine pathophysiology is multifactorial and complex. The thalamic and thalamocortical activity has been shown to play an essential role in the pathophysiology of migraine. Sleep spindles are an electroencephalographic (EEG) characteristic marker of non-rapid eye movement (NREM) sleep and associated with thalamus and thalamic connections. There are some studies which have evaluated EEG in migraine patients, not paying attention to sleep spindles. In the present study, we aimed to examine a possible thalamic network dysfunction by using the sleep spindles, in patients with migraine headache.
Methods: A retrospective study with a total of 17 children and adolescents with migraine and 15 age-matched controls were included. Their EEG data were investigated, and the amplitude, frequency, and duration of sleep spindles were evaluated.
Results: Our cohort consisted of 32 individuals. The median age was 15.5 years and 14.9 years in the migraine group and in the control group, respectively. Average, slow, and fast sleep spindle amplitudes were statistically higher in patients with migraine (p-values of 0.020, 0.013, and 0.033, respectively). Compared to the control group, the frequency of the fast sleep spindles was lower in the migraine group (p=0.03). Multivariate logistic regression analysis revealed an increased risk of migraine associated with increased average spindle amplitude and decreased fast spindle frequency and fast spindle duration.
Conclusion: Impairment in sleep spindles can reveal thalamic dysfunction in migraine patients. This may serve as an inexpensive and easily accessible method for early diagnosis of migraine. Further studies with sleep spindles can contribute to enlightening the pathophysiology of migraine.

Poster No. 139
The role of imaging in pediatric patients with chronic headache: relieving parent anxiety as secondary outcome

L BAKER, S ALTARAQJI, R ALSHAMI
Hamad Medical Corporation, Hamad General Hospital, Pediatric Neurology, Doha, Qatar

Background: Headache is one of the most common disorders in childhood. Up to 75% of young people report headache by the age of 15 years. 10% of school age children experience recurrent headache. The vast majority of recurrent headache is primary in origin, with estimated prevalence rates of migraine and tension-type headache of up to 9% and 24% respectively. Headache can have a significant impact on the quality of life of children, in part due to the unpredictability and unpleasant nature of attacks, but also due to the effect on day to day functioning such as concentration, school performance and attendance, and social/leisure activities, all these lead to increase the pressure for secondary care referral and request for unnecessary investigations. In general brain imaging should be performed only in children with abnormal findings on physical examination. But sometimes done to decrease the worries of their parent. This result was a secondary outcome from the primary research "The role of imaging in pediatric patient with chronic headache" which was accepted in 2016 with MRC#16159 in Hamad Research Centre.
Material: and *Methods:* A retrospective study for all the pediatric cases referred to pediatric neurology clinic with headache and normal neurological exam for who an imaging study was performed upon the parent pressure to relieve their worries were during 2015, all their record were reviewed including their follow up visit and ED visit for headache related complaint.
Results: 54 (77%) cases of total 70 patients in pediatric age group range between (3–18 years) old who had history of chronic headache with normal neurological examination and normal imaging done for headache never attend the emergency or request a secondary medical advice for headache following the explanation of the result of the imaging and assuring their parent.
Conclusion: In the vast majority of cases the young people who come to our clinics do not need further investigation. A clear history, the absence of clinical signs, and no red flag features usually means that we can proceed on the basis of a diagnosis of a primary headache disorder with some confidence. But despite many international guidelines designed to inform clinicians' decision-making with respect to neuroimaging there is increasing use of brain imaging in headache over recent years especially in pediatric cases, parents of the pediatric patient with headache might be frightened that their headache is caused by a brain tumor or another serious disorder. The majority of imaging results in patients with headache were normal or with benign lesions However doing imaging for young children with chronic headache in addition to good explanation of the symptoms for both the child and their parents greatly re-assure their parent and care giver with an impact of decreasing the attendance to emergency and decrease the request for follow up visit for further medical advice. In pediatric age group the pressure by the parent to rule out serious causes is much higher so strong parent wish for clarification might make it reasonable to perform cerebral imaging to eliminate these possible causes and to appease the parent.

Poster No. 140
Triggers of childhood migraine

AJ AYUBI, JF CANLAS, MAS AHMED
Department of Paediatrics, Queen's University Hospital, Essex, UK

Objective: Currently, there is limited research into triggers of childhood migraine. The aim of this study was to identify trigger in young patients with migraine.
Methods: This is non-interventional hospital-based study of healthy patients (<17 years) with migraine. Patients must experience at least two attacks of migraine that almost always or often precipitate an attack of headache. Trigger was defined as any factor that on exposure leads to of a migraine attacks. We did not inquire about the duration, amount or severity of exposure of trigger factors. Also we did not break down figures regarding particular factor.
Results: In the present study, 362 migraineurs reported at least one factor that triggered an attack of acute migraine. In our cohort, we were able to identify in total 14 different triggers of migraine. Majority (n=263; 72%) patients reported one trigger. Table shows common triggers. Triggers included stress (n=89; 24.5%), loud noise (n=68; 19%), bright light (n=59; 16%), food items (n=44; 12%), and climate (n=34; 9%). Majority of patients with MA and those with MoW reported one trigger (71% vs. 74% respectively), and prevalent triggers in both groups are the same.
Comment: Interestingly, when analysing our findings and available data migraine triggers, there are similar themes, that migraine triggered by common factors despite different societies, climates and cultures. This raises questions regarding the mechanism of action of triggers. It is important for health workers to identify migraine triggers as education of patients, parents and teachers would play a major role in migraine prevention. Because drug preventive therapy of migraine, has adverse effects, lack of satisfied responses, poor-compliance, limitations that restrict their use in children, and no specific drug has yet been specifically designed to prevent migraine.

Poster No. 141
Incidental neuroimaging findings among pediatric age group with non-acute headache

L BAKER, R ALSHAMI, S ALTARAQJI, A MOHAMEDZAIN
Pediatric Neurology, Hamad General Hospital, Doha, Qatar

Background: Headache is the most often reported neurological symptom. Physicians are regularly confronted with the question of whether or not it is necessary to perform neuroimaging in order to confirm a distinct headache diagnosis. In the vast majority of cases the young people who come to our clinics do not need further investigation. A clear history, the absence of clinical signs, and no red flag features usually means that we can proceed on the basis of a diagnosis of a primary headache disorder with some confidence, however many parents are frightened that their children with chronic headache are suffering from a severe disease and therefore request further diagnostics. This result was a secondary outcome from a primary research "The role of imaging in pediatric patient with chronic headache" which was accepted in 2016 with MRC #16159 in Hamad Research Centre.
Material: and *Methods:* A retrospective study for all the pediatric cases referred to pediatric neurology clinic with headache and normal neurological exam for who an imaging study was performed upon the parent pressure to relieve their worries during 2015, excluding those with recommended clinical criteria to consider diagnostic neuroimaging, all their record were reviewed including their neuroimaging finding.
Results: Total of 41 pediatrics headache patients were reviewed, with age range from 3 to 14 years, Neuro-imaging results were categorized as normal, remarkable without the need for follow up, remarkable with follow up. 22/41 (53.65%) had a normal neuroimaging results, 10/41 (24.39%) have shown sinuses/adenoids/maxillary polyps involvement, 3/41 (7.31%) patients had non-specific white matter lesions and otherwise unremarkable study, 2/41 (4.87%) were found to have incidental cyst (arachnoid, left fossorial) in their imaging studies, 1/41 (2.43%) was found to have skull fracture, also 1/41 (2.43%) was found to have asymmetrical small left transvers and sigmoid sinuses (documented as normal variant), again 1/41 (2.43%) was found to have incidentally a partial empty Sella (with normal shape and size of the pituitary gland), and lastly, 1/41 (2.43%) was found to have mastoiditis.
Summary: Headache is the most often reported neurological symptom. Physicians are regularly confronted with the question of whether or not it is necessary to perform neuroimaging in order to confirm a distinct headache diagnosis. In pediatric age group the pressure by the parent to rule out serious causes is much higher so strong parent wish for clarification might make it reasonable to perform cerebral imaging to eliminate these possible causes and to appease the parent. Unexpected results are frequently discovered in the course of medical testing including neuroimaging .our study showed that most of the incidental finding are remarkable variants of uncertain clinical significance .that confirm the lack of indication to perform neuroimaging for pediatric patient with non-acute headache and normal neurological examination.

Poster No. 142
Idiopathic intracranial hypertension service evaluation - review and recommendations

JD TARR, A DONALD, E KOTHANDARAMAN
Royal Manchester Children's Hospital, Manchester, UK

Objective: To review current practice and standard of care received by children with Papilloedema and Idiopathic Intracranial Hypertension. To develop a management guideline for IIH within a tertiary children's hospital.
Introduction: Incidence of IIH in UK paediatric population, although estimated to be 0.8 in 100,000, may be increasing with rising obesity levels. Children with IIH can present with symptoms of headache, visual difficulties and sometimes with other symptoms of raised intracranial pressure including Papilloedema. Evaluation commonly looks to not only confirm diagnosis but exclude other potential causes of raised ICP. Here, we reviewed the pathway from presentation to diagnosis of children presenting through Royal Manchester Children's Hospital General Paediatric department over an 18-month period with an aim of standardising and improving care received.
Method: Patients referred with papilloedema and those diagnosed with IIH were identified from General Paediatric admissions between January 2018 and June 2019 (n=34). From this cohort, 26 available case notes were reviewed. Investigations undertaken

and clinical documentation was reviewed against standards identified in literature recommendations.
Results: The review identified distinct variations in clinical practice in the investigations and management of patients presenting to the service and multiple referral routes. Five incorrect initial diagnoses were subsequently changed, four of which had already been commenced on unnecessary treatment. Time from presentation to management decisions ranged from 16 hours to 6 days. Diagnostic challenges resulted from delays in timely access to Paediatric Ophthalmology assessment and difficulties in lumbar puncture.
Conclusion: Following this review, we have developed a series of recommendations to improve practice including educational resources to increase success rates in lumbar puncture. A hospital wide guideline streamlining patient pathway across general paediatrics, paediatric ophthalmology and neurology services, offering clarity and standardisation in patient experience has been developed to minimise delays in diagnosis.

Poster No. 143

A case of idiopathic intracranial hypertension following spinal surgery for scoliosis

A HENDERSON[1], A KHAN[4], I SIMMONS[3], H CLIFFE[2], K PYSDEN[1]
[1]Department of Paediatric Neurology, Leeds Teaching Hospitals Trust, Leeds, UK; [2]Department of Radiology, Leeds Teaching Hospitals Trust, Leeds, UK; [3]Department of Opthalmology, Leeds Teaching Hospitals, Leeds, UK; [4]Department of Paediatric Spinal Surgery, Leeds Teaching Hospitals, Leeds, UK

Background: Idiopathic intracranial hypertension (IIH) is defined as an "increased intracranial pressure without hydrocephalus or mass lesion and with normal CSF composition". IIH is rare in children although the true incidence is unknown.
Case: A 13 year old girl following a musculoskeletal back injury, was found to have a clinically significant thoracolumbar double curvature scoliosis. She underwent primary posterior decompression and intertransverse fusion of the lumbar spine with primary fusion of the thoracic spine. A week postoperatively she developed vomiting, frontal headaches, double vision, and visual blurring. Assessment by ophthalmology revealed grade 3 optic disc swelling with associated splinter haemorrhages, and a bilateral sixth nerve palsy. MRI and MRV demonstrated prominence of the CSF sheath around the optic nerves but was otherwise normal. A lumbar puncture was performed with an opening pressure of 39cm H2O. Symptoms resolved post lumbar puncture. Acetazolamide was started and 6 months later her symptoms have resolved, there was no evidence of papillodema, and her vision returned to normal. Acetazolamide was weaned and she has remained well.
Discussion: There have been few reports of IIH following spinal surgery in children. One case series in 2011 reports three children who developed IIH around 2 weeks after elective spinal surgery. They suggested this may have been due to structural venous outflow changes or hyperfibrinogenemia following administration of ε–aminocaproic acid. This however was not used in this case. There have been no other reported cases in children, and only a few reports in adults. Although rare, it is important to consider IIH as a differential in patients presenting with symptoms of raised intracranial pressure following spinal surgery, and to undergo prompt ophthalmology review to ensure irreversible eye changes are prevented.

Poster No. 144

Retrospective analysis of phenotype and response to treatment in children with idiopathic intracranial hypertension (IIH) in the East of England (EOE) region diagnosed by ophthalmological or CSF studies

LD PERRY[1], H AKBARI[1], P HARIJAN[1], B MUTHUSAMY[2], S WHYTE[1], D KRISHNAKUMAR[1]
[1]Department of Paediatric Neuroscience, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; [2]Department of Ophthalmology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Objective: Evaluate the phenotype and response to treatment of children with IIH within the EOE region.
Methods: We retrospectively reviewed all referrals for suspected IIH in the EOE region over a 2-year period (August 2018–August 2020) evaluating demographics, phenotype, treatment(s) and symptom(s) resolution.
Results: There were 92 referrals; 19 (20.7%) diagnosed as IIH based on; infusion study 17 (89.5%); manometry at lumbar puncture 2 (10.5%). Mean opening pressure 23.96mmHg (SD +/- 5.27), mean plateau pressure 31.53mmHg (SD +/- 8.35). 3 were treated after failed CSF studies (3.3%). 12 (63%) were female; mean age 10 years (SD +/- 3.5); Mean BMI 25.15 (SD +/- 8.25), severely obese 2 (10.5%), obese 3 (15.8%), overweight 1 (5.3%) normal/low BMI 13 (68.4%). Presenting symptoms included headache (94.7%), visual disturbance (31.6%), nausea/vomiting (26.3%), dizziness (10.5%), abducens nerve palsy (10.5%), neck pain (5.3%), asymptomatic (5.3%). All had normal haematological investigations, papilledema (bilateral in 18, 94.7%) and MRI/MRV imaging excluding alternative diagnoses. Frisen grading was recorded in 14 (73.7%); grade 3–5 9 (64.3%); mild/grade 1–2 in 42.1% of all cases. Abnormal visual function was confirmed in 7 (36.8%). MRI findings of raised intracranial-pressure (ICP) were present in 12 (63.2%); compression of transverse sinuses 7 (58.3%), thickened optic nerve sheaths 5 (41.7%), flattened/empty sella 3 (25%). Treatment was with acetazolamide 11 (57.9%), topiramate 4 (21%), dual therapy 4 (21%); One child required a ventriculoperitoneal shunt. Symptom resolution occurred in 13 (68.4%) with improvement in the severity of papilledema in 16/17 cases with follow-up data (94.1%).
Conclusions: Most cases were female and only 31.6% were classified as overweight/obese. Common presenting symptoms include headache and visual disturbance and MRI signs of raised ICP were present in approximately 2/3 of cases. Visual function was affected in just over 1/3. Complete resolution of symptoms was achieved in approximately 2/3 of cases.

Poster No. 145

A tale of two movement disorders

JD SYMONDS[1,2], KS ELLIOTT[3], S MACLEOD[1], C MIGNOT[4], A ISAPOF[14], B KEREN[4], YA ZARATE[5], K PARK[6], M SAENZ[7], K BROWN[7], S JOSS[8], M CALLAGHAN[9], L HENDERSON[15], I CUTCUTACHE[10], M PAGE[11], M ARMSTRONG[11], H ASHRAFIAN[12,13], JC KNIGHT[3], SM ZUBERI[1,2]

[1]Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, UK; [2]Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK; [3]Wellcome Centre for Human Genetics, University of Oxford, Oxford, UK; [4]Sorbonne Université, Département de Génétique, Groupe Hospitalier Pitié-Salpêtrière-Hôpital Trousseau, Paris, France; [5]Section of Genetics and Metabolism, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [6]University of Colorado, Anschutz Medical Campus/Children's Hospital Colorado, Aurora, CO, USA; [7]Department of Pediatrics, Section of Genetics and Children's Hospital Colorado, Aurora, CO, USA; [8]West of Scotland Regional Genetics Service, Queen Elizabeth University Hospitals, Glasgow, UK; [9]Department of Paediatrics, University Hospital Wishaw, Wishaw, UK; [10]UCB Pharma, Slough, UK; [11]UCB Pharma, Braine l'Alleud, Belgium; [12]Division of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, UK; [13]Department of Experimental Therapeutics, Radcliffe Department of Medicine, John Radcliffe Hospital, Oxford, UK; [14]Sorbonne Université, Service de Neuropédiatrie, Hôpital Trousseau, Paris, France; [15]GeneDx, Gaithersburg, MD, USA

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 146

Epilepsy12: improving care for children with epilepsy

C DUNKLEY[1,2], C DOWN[2], F CALVIN-MWINGIRWA[2], M DAVID-FEVECK[2], H STACEY[2]

[1]Paediatrics, Sherwood Forest Hospitals NHS Foundation Trust, UK; [2]Epilepsy12, Royal College of Paediatrics and Child Health, UK

Objective: The Epilepsy12 audit was established in 2009 and aims to support services, and those who commission them, to measure and improve the quality of care for children and young people (CYP) with seizures and epilepsies.
Methods: Epilepsy12 collected data from Trusts/Health Boards in England and Wales about the organisation of their paediatric epilepsy services in November 2019; providing a comparison to historic Epilepsy12 data. Clinical data described the diagnosis, care and outcomes after 12 months for defined individual CYP having a first paediatric assessment July – November 2018.
Results: Organisational and clinical data was obtained from 136 and 113 Trusts/Health Boards respectively. Complete clinical data was obtained from 3318 CYP meeting inclusion criteria. More children and young people are receiving input from paediatricians with expertise and epilepsy specialist nurses; access to paediatric neurology where indicated remains static. There is an apparent reduction in CYP misdiagnosed with epilepsy. There was a clear reduction in sodium valproate use in females compared to males after age 9 years, and evidence that associated risks are discussed. Only 30% of children who met Children's Epilepsy Surgical Service (CESS) referral criteria were referred. Few Trusts and Health Boards provide co-located mental health services or screening for CYP with epilepsy. There was a very small and lower than expected number of CYP with an identified mental health condition.
Conclusions: There continues to be significant improvements in epilepsy care and services although there are still areas for improvement. There appears to be a shortfall in access to mental health and paediatric neurology and also CYP missing access to surgical evaluation. There is no room for complacency and whilst much resource is needed to be directed towards the current Coronavirus pandemic, we must also continue to transform services and approaches for children with epilepsies and their families.

Poster No. 147

Profound reduction in seizure frequency (≥75%) leads to improved everyday executive function: results of ZX008 (Fenfluramine) in Dravet syndrome

JH CROSS[1], K BISHOP[2], P ISQUITH[3], G GIOIA[4], G MORRISON[5], A GAMMAITONI[5], D HANEY[5], R NABBOUT[6], T POLSTER[7], JE SULLIVAN[8]

[1]UCL Great Ormond Street Institute of Child Health, Great Ormond Street Hospital, London, UK; [2]Global Pharma Consultancy, LLC Muncy, USA; [3]Boston Children's Hospital, Harvard Medical School, Boston, MA, USA; [4]Children's National Health System Rockville, Rockville, MD, USA; [5]Zogenix Inc, Emeryville, CA, USA; [6]Hôpital Universitaire Necker, Service de Neurologie Pédiatrique Centre de Référence Épilepsies Rares Paris, France; [7]Epilepsiezentrum Bethel, Krankenhaus Mara, Kinderepileptologie, Bielefeld, Germany; [8]University of California, San Francisco Benioff Children's Hospital, San Francisco, CA, USA

Objective: Patients with Dravet syndrome (DS) often experience executive function (EF) deficits. *Objective:* is to evaluate: (1) relationship between changes in convulsive seizure frequency (CSF) and EF and (2) impact of reducing CSF by comparing subsets of patients who experienced profound (≥75%) vs minimal (<25%) reductions after 1 year of add-on FFA in an open-label extension (OLE) study.
Methods: DS-patients entered the OLE (NCT02823145) of RCT (NCT02682927/NCT02826863) and completed an additional year of FFA, titrated to effect (0.2–0.7mg/kg/day; max 17mg/26mg/day with/without stiripentol). Percent difference in CSF per 28 days was calculated from baseline in the RCT. EF was evaluated with the Behavior Rating Inventory of Executive Function (BRIEF/BRIEF2) and the association between four indices/score (BRI, ERI, CRI, GEC) by Spearman's Rho correlation coefficients.
Results: 53 patients had a median % change in CSF of –71.0% (range, –99.7% to –55.0%). Responder analysis showed that 24/53 (45%) patients achieved a ≥75% reduction in CSF and 11/53 (21%) had <25% reduction. Change in CSF correlated significantly with ERI ($p=0.032$) and GEC ($p=0.034$). A significantly higher percentage of patients in the profound (≥75%) responder group experienced significant, clinically meaningful improvements on ERI and GEC ($p<0.05$).
Conclusion: There is a significant association between decrease in CSF and improvement in EF. A profound (≥75%) reduction in CSF resulted in significantly more patients experiencing clinically meaningful improvements in EF, suggesting that higher levels of CSF reduction for prolonged periods of time (≥1 year) may improve some EF deficits.

Poster No. 148

ZX008 (Fenfluramine) provides clinically meaningful reduction in seizure frequency irrespective of concomitant AEDs commonly used in Dravet syndrome

S ZUBERI[1], K KNUPP[2], L LAGAE[3], E THIELE[4], R NABBOUT[5], B GALER[6], G FARFEL[6], A GAMMAITONI[6]

[1]Royal Hospital for Children, Glasgow, UK; [2]University of Colorado, Children's Hospital Aurora, Aurora, CO, USA; [3]University of Leuven, Leuven, Belgium; [4]Massachusetts General Hospital Boston, Boston, MA, USA; [5]Hôpital Universitaire Necker, Service de Neurologie Pédiatrique Centre de Référence Épilepsies Rares Paris, France; [6]Zogenix Inc, Emeryville, CA, USA

Objective: Patients with Dravet syndrome (DS) often require multiple concomitant antiepileptic drugs (AEDs) for seizure management. The objective was to evaluate the efficacy of add-on fenfluramine (ZX008) in different combinations of commonly used concomitant AEDs in DS: stiripentol, clobazam, and/or clobazam/valproate.

Methods: DS-patients (ages 2–18 years) were included from two double-blind, parallel-group, placebo-controlled phase 3 studies (NCT02682927/NCT02826863; NCT02926898). Patients received ZX008 doses ranging from 0.2 to 0.7mg/kg/day (maximum daily doses: 26mg/day without stiripentol and 17mg/day with stiripentol). Percent difference in mean convulsive seizure frequency per 28 days (MCSF) was calculated from baseline relative to the combined titration and maintenance periods. Differences among subgroups were statistically evaluated using a covariance model (ANCOVA; α=0.05).

Results: A total of 206 patients with DS were enrolled in the double-blind studies (placebo: n=84; 0.2mg/kg/day ZX008: n=39; 0.4mg/kg/day ZX008: n=43; 0.7mg/kg/day ZX008: n=40). ZX008 provided clinically meaningful relief in patients with or without stiripentol (change in MCSF from prerandomization baseline without stiripentol: 62.3%, p<0.001; with stiripentol: 54.0%, p<0.001); with or without clobazam (without clobazam: 57.2%, p<0.001; with clobazam: 52.4%, p<0.001), and with or without the combination of clobazam/valproate (without combination: 49.8%, p=0.004; with combination: 54.2%, p<0.001). ZX008 was generally well tolerated. The most common treatment-emergent adverse events were fatigue, somnolence, lethargy, and appetite suppression or hypophagia.

Conclusion: ZX008 provided consistent, clinically meaningful reductions in seizure frequency when added to AED regimens regardless of the use of the common AEDs stiripentol, clobazam, or clobazam/valproate.

Poster No. 149

Worldwide short course education programmes in paediatric epilepsies – Improving knowledge and changing attitudes and practice

A GIFFORD[3,4], PJ RODIE[2], J WILMSHURST[5,6], C DUNKLEY[1], F O'CALLAGHAN[7,8], M GRIFFITHS[9,10], M KIRKPATRICK[3,4]

[1]Sherwood Forest Hospitals NHS Foundation Trust, UK; [2]British Paediatric Neurology Association, London, UK; [3]University of Dundee, Dundee, UK; [4]NHS Tayside, Dundee, UK; [5]University of Cape Town, Cape Town, South Africa; [6]Red Cross War Memorial Children's Hospital, Cape Town, South Africa; [7]University College London, London, UK; [8]Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; [9]University of Liverpool, Liverpool, UK; [10]Alder Hey Children's NHS Foundation Trust, Liverpool, UK

Background: The British Paediatric Neurology Association's PET (Paediatric Epilepsy Training) programmes, with almost 15,000 participants across five continents, include a 1-day standardised course promoting evidence-based, safe practice delivered by a trained faculty to a target audience.

Objective: To measure improvement in paediatric epilepsy knowledge and change in attitude and clinical practice after course attendance.

Methods: An identical true/false knowledge quiz with clinical management scenarios was performed at the beginning and end of the day in 24 courses in 2018. Between April 2018 and March 2019, an "Attitudes and Practice" survey was sent to 1,361 attendees 6-months after their course.

Results: – Knowledge gain: 762 participants completed a pre/post quiz (93% response rate in high-income countries [HIC], 79% in low- and middle-income countries [LMIC]). The gain in knowledge was much greater in LMIC (66%-pre to 85%-post versus 85 to 91% HIC). Attitudes and Practice Survey: 365 responses were received (21% response rate in HIC, 24% in LMIC). 76% report PET changed their personal practice moderately or significantly, rising to 88% from LMIC. 81% were prompted to improve their clinical service for children with epilepsies with 16% from LMIC creating dedicated epilepsy clinics. Practice change varied. 46% in LMIC no longer prescribed anti-convulsant prophylaxis for febrile seizures compared to 2% in HIC and 52% now used status epilepticus guidelines for the first time compared to 6%.

Conclusion: PET is improving knowledge and changing the attitudes and practice of clinicians with the highest gains to be seen in LMIC. This data provides evidence for the effectiveness of short-course epilepsy education to improve the lives of children with epilepsies globally.

Poster No. 150

Long-term safety and efficacy of add-on Cannabidiol (CBD) for treatment of seizures associated with tuberous sclerosis complex (TSC) in an open-label extension (OLE) trial (GWPCARE6)

EA THIELE[1], EM BEBIN[2], F FILLOUX[3], P KWAN[4], R LOFTUS[5], F SAHEBKAR[6], S SPARAGANA[7,8], J WHELESS[9]

[1]Massachusetts General Hospital, Boston, MA, USA; [2]University of Alabama School of Medicine, Birmingham, AL, USA; [3]University of Utah School of Medicine, Salt Lake City, UT, USA; [4]Monash University and the University of Melbourne, Melbourne, Victoria, Australia; [5]GW Research Ltd, Cambridge, UK; [6]Greenwich Biosciences, Inc., Carlsbad, CA, USA; [7]Scottish Rite for Children, Dallas, TX, USA; [8]University of Texas Southwestern Medical Center, Dallas, TX, USA; [9]The University of Tennessee Health Science Center and Le Bonheur Children's Hospital, Memphis, TN, USA

Objective: In this 2nd interim analysis of an OLE trial (GWPCARE6/NCT02544763), we report safety (full follow-up) and efficacy (through 72 weeks) of add-on CBD for treatment of TSC-associated seizures.

Methods: Patients who completed a randomised controlled trial (RCT) could receive GW Pharmaceuticals' formulation of plant-derived highly purified CBD (100 mg/mL oral solution) in the OLE (titrated to 25mg/kg/day, or up to 50mg/kg/day). Primary endpoint: safety. Secondary endpoints: percent change in TSC-associated (countable focal or generalised) seizures, responder rates, and Subject/Caregiver Global Impression of Change (S/CGIC).

Results: Of 201 patients who completed the RCT, 199 (99%) entered the OLE. Median (range) age: 10.7 (1.1–56.8) years. Baseline median seizure frequency/28 days: 57 seizures. At this analysis, 12% of patients had completed treatment, 31% had withdrawn, and 57% were ongoing. OLE median (range) treatment 372 (18–1127) days. Mean (SD) modal dose: 28 (9) mg/kg/day. AE incidence: 94%; serious AE incidence: 26%; 8% discontinued treatment due to AE(s). Most common AEs (≥20%): diarrhoea (45%), seizure (28%), decreased appetite (23%), pyrexia (21%), and vomiting (20%). Seventeen (9%) patients had elevated ALT/AST >3×ULN; 12 were on concomitant valproate. No patient met Hy's law criteria for severe liver injury. There was 1 death due to cardiopulmonary failure, deemed not treatment related by the investigator. Median reductions in TSC-associated seizures (12-week windows through 72 weeks): 53%–75%. Seizure reductions were 54%–80% for patients with a modal dose ≤25mg/kg/day (n=145). ≥50%, ≥75%, and 100% responder rates were maintained up to 72 weeks, ranging 52%–63%, 29%–51%, and 6%–19%, across 12-week windows). Improvement on S/CGIC was reported by 85% and 89% of patients/caregivers at 26 and 52 weeks.

Conclusions: Add-on CBD treatment was well tolerated and produced sustained reductions in TSC-associated seizures for up to 72 weeks.

Poster No. 151

Acquired disturbances of motor speech in the developmental epilepsy clinic

MR EYRE[1], S ROSE[2], M CLARK[2]

[1]Paediatric Neurology, Great Ormond Street Hospital, London, UK; [2]Paediatric Neurodisability, Great Ormond Street Hospital, London, UK

Objective: Developmental language disorders and aphasia are well recognised in childhood epilepsy; acquired disturbances in motor-speech planning (dyspraxia) and execution (dysarthria) are less well understood. We aimed to characterise children with epilepsy and motor-speech regression.

Methods: Cases were retrospectively identified (clinic database: 2013–2019). Inclusion criteria: age 3 to 16 years at initial assessment; presentation with epilepsy and acquired motor-speech disorder. Exclusion: prior epilepsy surgery. Clinical assessments, speech videos and EEG reports were reviewed.

Results: Of 19 patients (10F/9M), 7 had Landau-Kleffner syndrome (3 GRIN2A-mutation), 6 Rasmussen's encephalitis (4 dominant-hemisphere), 3 other generalised epilepsies (2 myoclonic-astatic), 2 other focal epilepsies, and 1 valproate-induced regression. Median age at initial assessment was 6.4 years (range 3.2–14.5) and at speech regression was 5.4 years (2.5–11.9). 13 had video. 18/19 (95%) had clinical seizures (focal 68%, generalised 47%, age at onset 4yrs [0.4–11.3]). Speech regression occurred within 2 months of onset or peak seizure burden in 50%. EEG (19/19) revealed focal abnormalities (79%, predominantly fronto-central/centrotemporal), generalised discharges (58%) and CSWS (16%). SLT assessment (19/19) identified dysarthria (74%), phonological errors (42%), dyspraxia (32%) and stammer (16%). Dysarthria was associated with drooling (57%) and dysphagia (36%). Mean expressive-language standardised score at initial assessment was 70.8 (SD 14.9) and at follow-up was 77.6 (SD 24) (13 patients followed up, median 1.9yrs interval, range 1–6). Patients showing improvement in expressive language (9/13, 69%) were younger at seizure onset (3.3 vs 5.3yrs, p=0.048, Mann-Whitney U test). 4/4 (100%) with Rasmussen's (all post-hemispherotomy) had an expressive-language disorder at follow-up, versus 4/9 (44%) in the remaining. 10/13 (77%) showed improvement in motor-speech, but residual difficulties persisted in 92%, affecting speech intelligibility in 54%.

Conclusions: Epileptic motor-speech regression typically manifested as dysarthria and was often temporally associated with seizure activity. Bilateral central focal EEG abnormalities were common. Non-progressive aetiology and younger age at onset predicted better expressive-language outcome, likely reflecting capacity for language reorganisation. Motor-speech problems often improved, but rarely resolved.

Poster No. 152

Population study of death in children with epilepsy in Scotland

MP PENDLETON[1], LP PADOVANI[2], JS SHETTY[2], SZ ZUBERI[3], SM MCLEOD[3], IA ABU-ARAFEH[4], MC CALLAGHAN[5], AM MCLELLAN[2]

[1]Paediatrics, Victoria Hospital, Kirkcaldy, UK; [2]Paediatric Neurology, RHSC, Edinburgh, UK; [3]Paediatric Neurology, Royal Hospital for Children, Glasgow, UK; [4]Paediatrics, Forth Valley Royal Hospital, Larbert, UK; [5]Paediatrics, University Hospital Wishaw, Wishaw, UK

Background: Epilepsy is the most common serious neurological disorder in children. Mortality rates in children with epilepsy (CwE) are reported to be 10 times the normal population rate and death is attributable to both epilepsy-related causes and non-epilepsy causes. More detailed, prospectively collected data is required to establish rates of death in CwE, identify modifiable factors and tailor conversations with families about risk.

Objective: To establish rates and causes of death in CwE and rates of SUDEP in Scotland.

Methods: Scottish Paediatricians notified any death in a CwE (aged 2 weeks to 18 years) to the Scottish Paediatric Surveillance Unit via monthly email from December 2014 to May 2018. The investigating team (from Scottish Paediatric Epilepsy Network) sent a questionnaire to the notifying paediatrician to obtain further information. Rates of deaths in CwE were calculated using National Records for Scotland data.

Results: 55 children were notified, and 43 questionnaires completed. (4 patients reported by 2 different clinicians). 39 patients included in this analysis. Mean age of death was 10.2 years (range 0.5–18 years). Mortality for this cohort accounted for 6.5% of child deaths annually. There were 9 (23%) reported cases of SUDEP (3 definitive, 4 probable and 2 possible.) Socioeconomic deprivation was not significantly correlated with SUDEP. 93% experienced seizures in the previous year (50% daily seizures). The commonest cause of death was respiratory failure/pneumonia (51%). Death most commonly occurred in hospital (47%). 7 children had a genetic epilepsy diagnosis and 5 children had neurodegenerative diseases.

Conclusions: Childhood deaths in CwE account for 6.5% of childhood mortality in Scotland with respiratory failure/pneumonia the commonest cause of death and high rates of co-morbidities. SUDEP accounted for 23% of deaths and further analysis of these cases may provide further insights into any modifiable factors.

Poster No. 153

Improving patient experience: An innovative approach to the medium chain triglyceride (MCT) ketogenic diet

H CHAMPION, M CHITRE, Z DOWD, A MAW, N MILLS, APJ PARKER

Paediatric Neurology Department, Cambridge University Hospital, Cambridge, UK

Introduction: The 45% MCT Ketogenic Diet is an established efficacious therapy; however a recent UK survey suggested <10% of children starting Ketogenic Dietary Therapy commenced an MCT-based diet. The diet can be onerous for families to implement as all MCT, LCT (Long Chain Triglycerides), carbohydrate and fat adjusted protein portions should be weighed. Few foods are allowed freely.

Objectives: This retrospective study investigated whether liberalising the MCT diet negatively affects compliance, degree of ketosis achieved, clinical efficacy or body weight. Liberalisation allowed low carbohydrate and protein-based foods freely. Portions of LCT, carbohydrate (>5g) and MCT continued to be weighed according to the child's calculated allowance.

Methods: Case notes of 54 consecutive patients prescribed a 45% MCT diet were reviewed; the last 27 to follow the traditional MCT diet (MCT KD) and the first 27 following the more flexible approach (fMCT). There were no exclusions.

Results: Dietary compliance improved on the fMCT diet; 23/27 had excellent compliance compared to 15/27 of children following the MCT KD. Optimal ketone levels were achieved earlier and were stronger at 3 months on the fMCT diet compared to the MCT KD; 29.5% and 18.5% respectively. Improved seizure burden (>50% seizure reduction) at 3 months comparable; 12/27 on MCT KD compared to 13/27 on fMCT diet. Weight change and interquartile range were comparable with median weight Z score changes of 0.06 (MCT KD) and 0.05 (fMCT diet). However, the interquartile range of those following the fMCT diet indicated poorer weight gain in the first 3 months on therapy.

Conclusions: The fMCT diet is an agreeable alternative way to teach and implement the use of a 45% MCT KDT; parents found it easier to comply with and the efficacy, degree of ketosis and rate of weight gain were not compromised.

Poster No. 154

Efficacy of add-on cannabidiol (CBD) treatment in patients with Tuberous Sclerosis Complex (TSC) and a history of Infantile Spasms: post hoc analysis of Phase 3 Trial GWPCARE6

FJ O'CALLAGHAN[1], SP SPARAGANA[2,3], P KWAN[4], RP SANETO[5], JW WHELESS[6], K HYLAND[7], F SAHEBKAR[8]
[1]UCL Institute of Child Health, London, UK; [2]Scottish Rite for Children, Dallas, TX, USA; [3]University of Texas Southwestern Medical Center, Dallas, TX, USA; [4]Monash University and the University of Melbourne, Melbourne, Victoria, Australia; [5]Neuroscience Institute, Seattle Children's Hospital and University of Washington, Seattle, WA, USA; [6]The University of Tennessee Health Science Center and Le Bonheur Children's Hospital, Memphis, TN, USA; [7]GW Research Ltd, Cambridge, UK; [8]Greenwich Biosciences, Inc., Carlsbad, CA, USA

Objective: In this post hoc analysis of a phase 3, randomised, placebo-controlled trial (GWPCARE6/NCT02544763), we compared response to add-on CBD in patients with TSC and treatment-resistant epilepsy with and without IS history.
Methods: Patients received GW Pharmaceuticals' formulation of plant-derived highly purified CBD (100mg/mL oral solution) titrated to 25mg/kg/day (CBD25) or 50mg/kg/day (CBD50) or placebo for 16 weeks. Negative binomial regression effect modification analysis was used to assess whether IS history affected CBD efficacy.
Results: 138/224 (62%) patients had IS history. Median (range) age: 12.2 years (1.1–56.8) for patients with IS history, 10.5 years (1.6–55.8) for those without; 74% <18 years. Median (Q1, Q3) baseline monthly TSC-associated seizure frequency: 59 (28, 117) and 51 (29, 96) for patients with and without IS history. CBD reduced TSC-associated seizures vs placebo regardless of IS history (interaction p-value: 0.803 for CBD25, 0.561 for CBD50). For patients with IS history, percent reduction in seizures from baseline: 45% for CBD25, 43% for CBD50, and 23% for placebo; placebo-adjusted reduction (95% CI): 29% (6%–45%) for CBD25 and 25% (3%–43%) for CBD50. For patients without IS history, reduction was 54% for CBD25, 55% for CBD50, and 32% for placebo; placebo-adjusted reduction (95% CI) was 32% (5%–52%) for CBD25 and 34% (7%–54%) for CBD50. AE incidence: 93% for CBD25, 100% for CBD50, and 95% for placebo; 8 patients (11%) on CBD25, 10 (14%) on CBD50, and 2 (3%) on placebo discontinued treatment because of an AE. Most common AEs: diarrhoea and somnolence, occurring more frequently with CBD than placebo. ALT/AST elevations (>3×ULN): 9 (12%) patients on CBD25, 19 (26%) on CBD50, none on placebo; 79% were on concomitant valproate.
Conclusions: CBD produced consistent reductions in TSC-associated seizures in patients with and without IS history.

Poster No. 155

Longitudinal phase of a prospective open-label trial of mixed CBD/THC cannabis oil in pediatric patients with Dravet Syndrome

N KABIR[1], OC III SNEAD[1], M ZAK[1], B MCCOY[1,2]
[1]Division of Neurology, The Hospital for Sick Children Toronto, Canada; [2]Paediatric Neurology, Blackrock Clinic, Dublin, Ireland

Objective: The Cannabinoid trial was designed to determine the tolerability and optimal dose of a mixed CBD/THC Cannabis extract (TIL-TC150) as an adjunct treatment in children with severe drug resistant epilepsy due to Dravet Syndrome. Primary analysis at 20 weeks showed it to be safe and well tolerated in majority of participants and is previously published. This longitudinal phase (to 64 weeks) was a continuation of the trial to further assess safety and tolerability for participants who chose to continue with TIL-TC150 therapy, a cannabis plant extract produced by Tilray®, containing 100mg/mL CBD and 2mg/mL THC, beyond the primary analysis period.
Methods: Fourteen participants continued into the longitudinal phase of the study and were monitored for tolerability and adverse events to 64 weeks. In addition, quality of life assessment was completed at 52 weeks.
Results: Range of maximum dose of TIL-TC150 achieved at week 64 was 10 to 16mg/kg/day CBD. Mean dose achieved for the eleven participants at week 64 was 14.7mg/kg/day CBD. Seven participants (64%) reached the target dose of 16mg/kg/day CBD. Most common adverse events observed during the longitudinal phase beyond habitual seizures were reduced appetite and constipation. These were transient or resolved without dose change. There was a statistically significant improvement in quality of life at 52 weeks compared to baseline (59.1±20.2 vs 34.1±23.1, $p<0.05$). A median seizure reduction of 87.5% for motor seizures was observed in almost half of participants. One participant remained seizure free from primary analysis to longitudinal endpoint.
Conclusions: Analysis of the longitudinal phase of TIL-TC150 treatment for 64 weeks shows that treatment was safe and well tolerated in most children. Improved quality of life continued 1 year after starting cannabinoid therapy.

Poster No. 156

Use of lacosamide and outcomes in children and young people with epilepsy

A YULE, W WHITEHOUSE
Paediatrics, Queen's Medical Centre, Nottingham, UK

Objectives: Previously, our centre conducted an audit to determine how lacosamide was used within our patient population. We have updated this and aim to demonstrate the relationship between dose, serum concentration, and reduction in seizure frequency in our patients.
Methods: Retrospective review of paediatric patients dispensed lacosamide through our pharmacy between January 2016 - August 2019. We reviewed patient notes and letters to establish seizure type and clinical outcome ≥12 months after starting lacosamide and compared this against hospital lacosamide serum concentrations.
Results: 89 patients were identified, however only 79 had sufficient documentation to be included. The median age was 7 years (range 1 day to 17 years), and 45/79 were males. 29/79 (37%) had focal epilepsies, 27/79 (34%) generalised, and 23/79 (29%) unclassified or mixed epilepsies. 30/79 (38%) had >50% seizure reduction at ≥12 months. The maximum recorded concentration of lacosamide (median maximum 8.5 mg/L) was proportional to the lacosamide dose (median 7.1mg/kg/day). Comparing the maximum doses given and concentrations achieved with efficacy (seizure frequency reductions), we found a negative relationship, as those without adverse effects who did not respond to low or moderate doses

were given increasing doses, with diminishing returns (correlation coefficients R=–0.45 and –0.28 respectively).
Conclusions: We use lacosamide for a wide variety of seizures and epilepsies in a wide range of doses, from neonates to teenagers. Higher doses, above 10mg/kg/day did not improve seizure frequency significantly in our small sample, even though we tried doses up to 26mg/kg/day. Similarly serum concentrations above 20mg/L were not associated with improved seizure frequency, although some patients had concentrations up to 27mg/L. In children without adverse effects, increasing lacosamide doses above 10mg/kg/day is unlikely to be beneficial.

Poster No. 157
Ictal EEG does not predict surgical outcome in children undergoing epilepsy surgery due to unilateral focal lesions on MRI

FC CASTRO[1,2], FM MOELLER[1,3], SP PUJAR[1,2], MT TISDALL[1,4], HC CROSS[1,2], CE ELTZE[1,2]
[1]Great Ormond Street Institute of Child Health, University College of London, London, UK; [2]Department of Neurology, Great Ormond Street Hospital, NHS Trust, London, UK; [3]Clinical Neurophysiology Department, Great Ormond Street Hospital, NHS Trust, London, UK; [4]Department of Neurosurgery, Great Ormond Street Hospital, NHS Trust, London, UK

Introduction: Epilepsy surgery is an evidence-based treatment for pharmacoresistant epilepsy. Current pre-surgical evaluation-practice includes ictal and interictal EEG for all patients. For patients with a clearly demarcated single unilateral structural lesion on MRI and location compatible seizures, it is unclear whether the ictal EEG recording is required for surgical decision making. We aimed to investigate the relationship between interictal, ictal EEG and seizure free outcome, and other clinically relevant predictors in this group.
Methods: Children undergoing epilepsy surgery at Great Ormond Street Hospital from 2012-2017 were included in a retrospective record review if they had a single, unilateral MRI lesion; pre and postsurgical data were obtained. Video-Telemetry was classified as localising/lateralising or non-concordant with the MRI lesion. The odds of seizure-free outcome were calculated between the non-concordant vs localising/lateralising interictal and ictal EEGs. Multivariable logistic regression was conducted to correct for confounders.
Results: Of 467 patients 106 fulfilled inclusion criteria, with the following histopathologies: Tumours 46 (43%), Focal Cortical Dysplasia 28 (26%), Mesial Temporal Sclerosis 23 (21.6%), and others 9 (8.4%). 73/106 (69%) were seizure free at last follow-up (median 26 months, IQR 17–37.5). Seizure persistence was predicted by a non-concordant interictal EEG (OR=0.215, CI 0.078 to 0.598, p=0.002) and a non-concordant ictal EEG (OR=0.598, CI 0.123 to 0.796, p=0.022). In the logistic regression analysis correcting for confounders, the 'non-concordant interictal EEG' remained independently associated with seizure persistence (OR=0.265, CI 0.085 to 0.265, p=0.022), whilst 'non-concordant ictal EEG' was no longer significant (OR =0.313, CI 0.191 to 1.57, p=0.264). Other negative prognostic factors were developmental delay/intellectual disability, higher number of preoperative antiepileptic drugs and incomplete resection.
Conclusions: Our findings questioning the mandatory requirement of ictal EEG for pre-surgical evaluation for patients with single unilateral MRI lesions may require validation in a larger cohort and prospective study design.

Poster No. 158
Epilepsy and long-term developmental trajectories in SCN2A-related epilepsies

RN MENON[1,2], H RICHARDSON[2], S AYLETT[2], S BHATE[2], M CLARK[2], K DAS[2], C ELTZE[2], M KALIAKATSOS[2], R ROBINSON[2], S VARADKAR[2], G CHOW[3], J PATEL[6], K LASCELLES[5], N ISMAYILOVA[7], F ELMSLIE[4], E HUGHES[5], A WHITNEY[8], A KUMAR[2], M KURIAN[2,9], JH CROSS[2,9], A MCTAGUE[2,9]
[1]Neurology, SCTIMST, Thiruvananthapuram, India; [2]Great Ormond Street Hospital, London, UK; [3]Nottingham University Hospitals, Nottingham, UK; [4]St Georges University Hospital, London, UK; [5]Evelina London Children's Hospital, Guy's & St Thomas', London, UK; [6]Bristol Royal Hospital for Children, Bristol, UK; [7]Chelsea & Westminster Hospital, London, UK; [8]University Hospital Southampton, Southampton, UK; [9]UCL Institute of Child Health, London, UK

Objective: Heterozygous pathogenic variants in SCN2Aare an important cause of the developmental-epileptic encephalopathies (DEEs) of infancy and early childhood. In this retrospective case-note analysis, we aimed to investigate predictors of and relationship between long-term seizure and developmental outcomes.
Methods: A review of the hospital records of children who underwent comprehensive evaluation and next generation sequencing demonstrating ACMG class 4 or 5 variants in the SCN2A gene was conducted. A follow-up period of 1 year with developmental information was mandatory for inclusion.
Results: Twenty nine of 52 children with SCN2A-related epilepsy had long term developmental data documented on serial follow-up. Early infantile-onset epilepsy (<6 months) was noted in 25 (86.2%) with 19 (65.5%) presenting as neonatal-onset epilepsy. Electro-clinical diagnosis at baseline included focal epilepsy in 14 (48.3%), DEE with suppression burst in 8 (27.6%), West syndrome in 2 (6.9%), epilepsy of infancy with migrating focal seizures in 2 (6.9%) and self-limited familial epilepsy in 3 (10.3%). Global developmental delay was apparent in 21 (72.4%) with co-existent autism in 8 (27.6%) and specific language, learning or social communication disorder in 4 (13.8%). Neurological deficits included spasticity in 14 (48.3%), cortical visual impairment in 8 (27.6%) and movement disorders in 9 (31%). One patient had a co-existent malformation of cortical development (MCD). Neonatal onset DEE was associated with more significant developmental delay and inter-ictal EEG abnormalities at baseline. Factors associated with long-term seizure freedom included early genetic diagnosis, low seizure frequency at 1 year of follow-up, less developmental lag at last follow-up, family history of seizures, absence of epileptic spasms and response to sodium channel blocking drugs, especially carbamazepine.
Conclusions: SCN2A-related epilepsy is an important cause of DEE with heterogeneous phenotypes, resulting in significant morbidity. Early genetic diagnosis can improve seizure outcomes but this may not necessarily translate to normalisation of the developmental trajectory.

Poster No. 159

Patient survey of epilepsy virtual clinics during the COVID 19 pandemic

D HANNA, MY LAC, K LASCELLES, E HUGHES, R WILLIAMS, S TANG

Children's Neurosciences, Evelina London Children's Hospital, Guys and St Thomas' Hospital, London, UK

Objective: Due to the COVID 19 pandemic, the paediatric complex epilepsy service changed rapidly from face to face clinics to virtual clinics. The Evelina London Complex epilepsy team was involved in the RCPCH EQIP collaborative pilot, our project was adapted to investigate patient experience and satisfaction for Virtual consultation.
Methods: We designed a questionnaire consisting of 19 questions. 15 were multiple choice questions and three were qualitative. Patients were selected randomly from virtual clinic booking lists from March to July 2020. The questionnaires were completed using telephone interview with parents.
Results: We obtained feedback from 20 families. Response rate was 100%. 17/20 (85%) of the responders rated the quality of virtual consultations compared with face to face as good (n=11) and excellent (n=6). Similarly, 17/20 (85%) were very satisfied (n=10) or satisfied (n=7) with virtual consultations. 14/20 (70%) responders felt it respected confidentiality. However 5/20 (25%) responders reported technical issues during the consultation. Given a choice on ongoing epilepsy consultations, 8/20 responders preferred to continue virtual consultations, 6/20 would prefer face to face appointments, 5/20 chose both virtual and face to face depending on the circumstances and 1/20 preferred a phone clinic. Qualitative feedback included "With face to face clinics my child gets a personal connection with the Consultant who can also examine her" Others supported virtual appointments "If routine check-up or discussion of seizure diary and management then virtual is easier" Responders gave suggestions for how their virtual experience can be improved.
Conclusion: Virtual clinic consultations are usually acceptable to parents. Our survey demonstrates that the majority of families would also like to have a continued option for a face to face clinic and it highlighted improvements that can be made with virtual consultations. Continued survey of parent/carers and patients throughout the pandemic and beyond will aid to inform organisation of outpatient epilepsy services.

Poster No. 160

Childhood epilepsy with centrotemporal spikes: epidemiology, neurocognitive impairment and the investigation of sensorimotor cortical dysfunction

J TE WATER NAUDE[1], A SAXENA[1], F GIBBON[1], A KIRBY[2], K HAMANDI[3]

[1]Child Health, Children's Hospital for Wales, Cardiff, UK; [2]Dyscovery Centre, University of South Wales, Newport, UK; [3]Neurology, University Hospital of Wales, Cardiff, UK

Objective: Childhood epilepsy with centrotemporal spikes is said to be one of the more common childhood epilepsy syndromes: we performed a study investigating this in Wales over a 33-month period. The other objective was investigating whether there were correlates between the neurocognitive phenotype and advanced imaging techniques.
Methods: We used the established methodology of the Welsh Paediatric Surveillance Unit to ascertain the incidence of this epilepsy syndrome in Wales. Twenty-one children with this syndrome were recruited to a parallel study which used standardised assessments for language, cognition, motor function and handwriting, as well as advanced imaging techniques (high resolution cranial magnetic resonance imaging (MRI) and magnetoencephalography (MEG) with a simple motor paradigm) to define any correlation between the defined behavioural phenotypes with the MEG oscillatory background and movement-induced sensorimotor responses.
Results: The incidence of this condition in Wales was under 3 cases per 100,000 children aged 1 to 14 years, which is significantly lower than that reported for this epilepsy syndrome. Ninety percent of the group who were intensively studied showed some difficulties in at least one area of function using standardised assessment tests, especially in one or more areas of motor dysfunction. In the sensorimotor network, MEG suggested a greater variability in oscillatory amplitude compared to controls, whereas there was no difference in the visual network. There was also a reduced ipsilateral movement-related beta desynchrony in this region in affected children.
Conclusions: This epilepsy syndrome is not common in Wales. Most children with this disorder have a heterogeneous pattern of neurocognitive impairments, especially motor difficulties (associated with altered motor-related oscillatory responses in the ipsilateral motor cortex). Our results point toward a "disorganized" functional sensorimotor network, underlying this syndrome.

Poster No. 161

Long-term (2-year) safety and efficacy of adjunctive ZX008 (Fenfluramine) for Dravet syndrome: Interim results of ongoing open-label extension study

S ZUBERI[1], M PRINGSHEIM[2,3,4], L LAGAE[5], R NABBOUT[6], G FARFEL[7], B GALER[7], G MORRISON[7], M LOCK[7], A GAMMAITONI[7], A MISTRY[7]

[1]Royal Hospital for Children, Glasgow, UK; [2]Schön Klinik Vogtareuth, Kinder und Jugendneurologie, Vogtareuth, Germany; [3]Paracelsus Medizinische Privatuniversität Salzburg, Austria; [4]Deutsches Herzzentrum München, Germany; [5]University of Leuven, Leuven, Belgium; [6]Hôpital Universitaire Necker, Service de Neurologie Pédiatrique Centre de Référence Épilepsies Rares Paris, Paris, France; [7]Zogenix Inc, Emeryville, CA, USA

Objective: A previous interim analysis demonstrated clinically meaningful (≥50%) reduction in monthly convulsive seizure frequency (MCSF) in 64.4% of patients with Dravet syndrome (DS) after a median 256 treatment days with Fenfluramine added to existing antiepileptic therapy. The objective is to evaluate the long-term safety and efficacy of ZX008 after up to 2 years.
Methods: Patients completing phase 3 studies enrolled in an open-label extension (OLE) study (NCT02823145). Starting at 0.2mg/kg/day ZX008 patients were titrated to max 0.7mg/kg/day or 26mg/day (or 0.4mg/kg/day, 17mg/day with stiripentol). Seizure frequency was captured via hand-held e-diary. Effectiveness and safety were assessed at each visit.
Results: At time of analysis (2/15/2019), 330 patients were enrolled (mean±SD age: 9.0±4.6 years old [y/o]; 55% male; 28% <6y/o), with a median treatment duration of 445 days (range: 7–899 days). At 2 years on treatment, median MCSF change was –83.3% compared with the pre-fenfluramine treatment, core-study baseline

(p<0.001). Over the entire treatment period, 62% of patients experienced clinically meaningful (≥50%) and 37% experienced profound (≥75%) reductions in MCSF. Most common (≥15%) TEAEs were nasopharyngitis (23%), pyrexia (23%), decreased appetite (21%), and diarrhoea (15%). There were no echocardiographic or clinical observations of valvular heart disease or pulmonary hypertension at any time during the OLE.
Conclusion: Fenfluramine provided durable, clinically meaningful reduction in MCSF for up to 2 years of treatment and was generally well tolerated. ZX008 may represent an important new treatment option for patients with DS.

Poster No. 162
Infantile spasms in Trisomy 21: A review of current treatment approach and outcomes in Ireland

S HARVEY[1], K FLYNN[1], C LEAHY[1], M EL HASSAN[2], J AZIZ[5], C KEHOE[6], N LYNCH[3], E O'MAHONY[4], N MCSWEENEY[5], O O'MAHONY[5], N ALLEN[6,7], S TIRUPATHI[8], D HANRAHAN[8], J C MCHUGH[2], D WEBB[2], M O'REGAN[2], A SHAHWAN[1], D O'ROURKE[1,9], B LYNCH[1], M KING[1,9], K GORMAN[1,9]
[1]Childrens Health Ireland at Temple Street, Dublin, Ireland; [2]Childrens Health Ireland at Crumlin, Dublin, Ireland; [3]Bon Secours Hospital, Cork, Ireland; [4]University Hospital Limerick, Limerick Ireland; [5]Cork University Hospital, Cork, Ireland; [6]Galway University Hospital, Galway, Ireland; [7]National University of Ireland Galway, Galway, Ireland; [8]Royal Belfast Hospital for Sick Children, Northern Ireland, UK; [9]University College Dublin, Dublin, Ireland

Objective: Ireland has one of the highest incidences of Trisomy 21 in Europe (1 in 411 live births). Infantile spasms (IS) are identified in 0.6 to 13% of children with Trisomy 21 and are associated with poorer neurodevelopmental outcomes, increased epilepsy risk and autism spectrum disorders. Internationally, first-line treatment varies due to resource availability, physician preference and cost. Studies to date largely report on ACTH and Vigabatrin use. Reported outcomes are variable with relatively small cohorts, making it difficult to ascertain valuable conclusions to inform clinical practice.
Methods: A 10-year retrospective multi-centre review of cases of IS in children with Trisomy 21 involving all seven paediatric neurology centres in Ireland. Clinical records, electroencephalogram (EEG), and imaging reports were reviewed.
Results: 54 infants identified with median IS onset age of 6 months 2 days (4–33 months). Prednisolone was the most common first-line medication (n=20), followed by Vigabatrin (n=19), Sodium Valproate (n=9), combined Prednisolone/Vigabatrin (n=5) and ACTH (n=1). Following first-line medication only, spasm cessation was recorded in 11/20 Prednisolone, 5/19 Vigabatrin, 1/9 Sodium Valproate and 4/5 Prednisolone/Vigabatrin. Following first-line choices effective further medications included Vigabatrin, Sodium Valproate and Zonisamide with cessation in 4/13, 5/15 and 5/8 respectively. Mean number of medications required for spasm cessation was 2.4 (1–10). At follow-up, 85% of infants had experienced spasm resolution, 19% had ongoing seizures and there were developmental concerns in 83% with severe global delay in 17%. Median time to spasm cessation from onset was 116 days (5–116 days). Eighteen children experienced side-effects from medication, with Vigabatrin accounting for 48% of reported side-effects.
Conclusion: Prednisolone is an effective medication which is well tolerated. Although success is seen with ACTH (n=1) and combination Prednisolone/Vigabatrin (n=5), numbers are small. Potential second-line options include Vigabatrin, Sodium valproate and Zonisamide. There was a high reported spasm cessation (85%) however developmental concerns and ongoing seizures occurred in a large number.

Poster No. 163
Long-term safety and efficacy of adjunctive Perampanel in paediatric patients (aged 4 to <12 years) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS) in study 311

R FLAMINI[1], A PATTEN[2], LY NGO[3]
[1]Pediatric and Adolescent Neurodevelopmental Associates, Atlanta, GA, USA; [2]Eisai Ltd., Hatfield, Hertfordshire, UK; [3]Eisai Inc., Woodcliff Lake, NJ, USA

Objective: Perampanel is a once-daily oral anti-seizure medication (ASM) for POS and PGTCS. Study 311 (NCT02849626) was a multicentre, open-label, single-arm study of perampanel oral suspension (0.5 mg/mL) in paediatric patients (aged 4 to <12 years) with POS (with or without secondarily generalised seizures [SGS]) or PGTCS. Here, we report long-term (1-year) 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 (23 weeks of treatment) and Extension Phase A (52 weeks 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 ASMs. 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: 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 (1-year) adjunctive perampanel is generally safe, well tolerated and efficacious in paediatric patients aged 4 to <12 years with POS (with or without SGS) or PGTCS.

Poster No. 164

Experiences and views of parents of school-aged children with epilepsy regarding educational and therapeutic supports

EC JOHNSON[1], JH CROSS[1,2,3], P ATKINSON[4], A MUGGERIDGE[1], C REILLY[1,2]

[1]Research Department, Young Epilepsy, Lingfield, UK; [2]UCL Great Ormond Street Institute of Child Health (ICH), London, UK; [3]Great Ormond Street Hospital for Children NHS Trust, London, UK; [4]Child Developmental Centre, Crawley Hospital, Crawley, UK

Objective: To gain an understanding of the views of parents of children with epilepsy regarding the process of securing educational and therapeutic supports and the changes they would like to make to this provision.
Methods: Parents (n=68) of children (born between 2003 and 2014) with 'active' epilepsy (at least one seizure in last year) resident in the RH10 to RH13 postcode areas of West Sussex, were interviewed using a semi-structured interview schedule The interviews were conducted between October 2018 and March 2020 and coded using Thematic Analysis by two independent raters.
Results: Parents reported difficulties accessing both educational and therapeutic supports. They often felt that they had to drive the process to gain supports themselves. They reported little professional support, and inadequate communication regarding their child's needs with school staff and between school staff and/or medical/therapeutic professionals. Parents of children with severe intellectual disability (ID) and/or who attended a special school generally reported finding the process easier. Parents of children with mild to moderate ID who attended mainstream schools reported the most difficulties. Regarding changes parents would like to make to their child's current educational and/or therapeutic supports, they highlighted the need for school staff to recognise the impact of epilepsy on learning and behaviour and to support their child more holistically. Many wanted greater access to assessment and therapeutic provision in relation to their child's learning and behaviour. They also highlighted the need for the child's schoolwork to be appropriate to their cognitive ability and profile.
Conclusion: Parents of school-aged children with epilepsy report difficulties accessing appropriate educational and therapeutic supports for their child and would like more support in the process. Parents also highlight the need for increased knowledge of the impact of epilepsy on learning and behaviour and want more resources for assessment in these areas.

Poster No. 165

Genetic generalised epilepsy in Okur-Chung neurodevelopmental syndrome

GR HUDSON[1], A MICHELL[1], R ROBERTS[2], L RHODES[3], K ANGIONE[4], A PARKER[1]

[1]Clinical Medical School, University of Cambridge, Cambridge, UK; [2]Rare and Inherited Diseases Lab, Great Ormond Street Hospital, London, UK; [3]Clinical Genomics and Research Programs, GeneDx; [4]University of Colorado, CO, USA

Objective: We report 2 cases of Okur-Chung Neurodevelopmental Syndrome (OCNS) with previously unreported genetic variants in CSNK2A1. The epilepsy type in OCNS has not been characterised. We report the genetic generalised epilepsy experienced by these children and offer a hypothesis for the mechanism of epileptogenesis.
Methods: We compared 2 children with OCNS, recording their phenotype, including seizures and EEG. We report genotypes of: patient 1 using whole genome sequencing (Genome quality score=99) confirmed with Sanger Sequencing, and patient 2 using exome sequencing (mean depth of coverage=144x, quality threshold=97.6%). We reviewed the published literature for any other characterisations of epilepsy type in OCNS.
Results: Patient 1 has a c.157 C>G mutation in the CSNK2A1 gene on chromosome 20p13 and patient 2 has a c.426+1 G>T mutation on intron 6 of the same gene- warranting diagnosis of OCNS. This is the first time either variant has been reported, both were heterozygous and de novo. In keeping with OCNS, patient 1 displays signs including poor speech/language development/coordination, microcephaly and short-stature. Contrastingly patient 2 is relatively spared, suffering only with significant learning difficulty. Both have epilepsy, with generalised spike-wave epileptiform activity on EEG at seizure onset. Seizure phenotype is varied including absence seizures, tonic seizures, atonic seizures and myoclonic absences in patient 1 and tonic and tonic-clonic seizures in patient 2. Both were refractory to pharmacological management, but partially responsive to ketogenic diet therapy (KDT).
Conclusions: Okur Chung Neurological Syndrome in these children was associated with drug resistant genetic generalised epilepsy, with some response to KDT. This could be related to CK2's role in regulating NMDA presence on the cell membrane. Given the variability of the dysmorphic features, CSNK2A1 should be sequenced in early onset genetic epilepsies of unknown cause.

Poster No. 166

Use of the ketogenic diet in difficult to treat epilepsy - an evaluation of efficacy and long-term tolerability

JD WILLIAMS[1,2], J BUTTLE[1], O MCGUINNESS[1], S BREMNER[1], SM ZUBERI[1,2], A BRUNKLAUS[1,2]

[1]Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, UK; [2]College of Medical, Veterinary & Life Sciences, University of Glasgow, Glasgow, UK

Objective: The ketogenic diet (KD) is known to be an effective treatment for difficult to treat epilepsy and GLUT-1 deficiency. Important side effects include dyslipidaemia and renal stones. Patients are often treated for 2 to 3 years, although some remain on KD for considerably longer. This study aimed to evaluate the KD's efficacy, as well as the factors associated with adverse effects in the long-term.
Methods: 49 children who had been on KD for at least 12 months between January 2015 to February 2019 were included in this study. Treatment efficacy and side effects were recorded via standardised proformas. Patients with renal stones were compared to those without, focusing on clinical information such as syndromic diagnosis, mobility levels, use of carbonic anhydrase inhibitors, laboratory values such as urine calcium-creatinine ratio, serum triglycerides and serum cholesterol.
Results: The KD had good efficacy with 91.7% of patients' parents/carers reporting at least 50% reduction in seizures. Six patients (12.2%) developed renal stones/nephrocalcinosis independent of clinical characteristics such as syndromic diagnosis or

mobility levels. Rates of high urine calcium-creatinine ratios were not significantly different between groups (renal stones 50% vs no renal stones 39.29%, p=ns). Equally, rates of high triglycerides did not differ between groups (50% vs 48.65%, p=ns). However, hypercholesterolaemia was more frequently seen in those with renal stones (50% vs 11.9%, p=0.05) and patients who were treated for longer than 5 years displayed a significantly higher rate of hypercholesterolaemia (44.44% vs 10.26%, p=0.031).
Conclusions: Although treatment efficacy of the KD is very encouraging, we encountered significant adverse effects including the formation of renal stones and hypercholesterolaemia. Longer-term patients may be at risk of hypercholesterolaemia and should be monitored for associated complications. Future work should seek to validate these findings and look for other potential associations that this study was unable to comment on.

Poster No. 167
Real-world experience of treating patients aged <12 years with Perampanel

S AUVIN[1], A GARCIA-RON[2], G ZIMMERMANN[3,4], T WU[5], W D'SOUZA[6], LY NGO[7], V VILLANUEVA[8]
[1]Service de Neurologie Pédiatrique, Hôpital Robert Debré, Paris, France; [2]Hospital Universitario Clinico San Carlos, Madrid, Spain; [3]Christian-Doppler University Hospital, Paracelsus Medical University, Centre for Cognitive Neuroscience, Salzburg, Austria; [4]Team Biostatistics and Big Medical Data, IDA Lab Salzburg, Paracelsus Medical University, Salzburg, Austria; [5]Chang Gung Memorial Hospital Linkou Medical Center and Chang Gung University College of Medicine, Taoyuan, Taiwan; [6]Department of Medicine, St Vincent's Hospital Melbourne, The University of Melbourne, Victoria, Australia; [7]Eisai Inc, Woodcliff Lake, New Jersey, USA; [8]Refractory Epilepsy Unit, Hospital Universitario y Politécnico La Fe, Valencia, Spain

Objective: To assess perampanel (PER) when used in everyday clinical practice in patients aged <12 years.
Methods: Patients aged <12 years with focal or generalised epilepsy treated with PER were identified from an interim pooled analysis of 18 global studies. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type at last visit. Effectiveness assessments included seizure freedom rate (no seizures since at least prior visit) and responder rate (≥50% seizure frequency reduction). Safety/tolerability assessments included adverse events (AEs) and AEs leading to discontinuation.
Results: Twenty-one patients aged <12 years were identified (50.0% male; mean age 7.4 years; mean epilepsy duration 5.3 years). Effectiveness was assessed for 17 patients; safety/tolerability for 12 patients. Seizure types at baseline were focal only (82.4%), generalised only (5.9%) and both focal and generalised (11.8%). Prior to PER initiation, mean number of antiepileptic drugs received was 5.4. Mean number of concomitant antiepileptic drugs was 2.3 at baseline and 2.8 at last visit. Mean PER dosage was 1.9mg/day at baseline and 4.5mg/day at last visit. At 3, 6 and 12 months, retention rates were 88.9% (8/9), 77.8% (7/9) and 66.7% (6/9), respectively. Reasons for discontinuation were lack of efficacy (n=2) and AEs (n=1). Mean time under PER treatment was 9.2 months. At last visit, seizure freedom and responder rates in patients with focal seizures were 27.3% and 54.5%, respectively; 18.2% had unchanged seizure frequency and no patient had seizure worsening. One patient had generalised seizures and experienced ≥50% seizure frequency reduction. AEs were reported for 50.0% of patients; most frequently were behavioural AEs (aggression/anger/irritability; 50.0%) and somnolence (16.7%).
Conclusions: PER was effective and generally well tolerated in clinical practice when used in patients aged <12 years with focal and generalised seizures.

Poster No. 168
Efficacy and safety of adjunctive Perampanel 4mg/day in paediatric patients (aged 4–<12 Years) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS) in Study 311

K MORETZ[1], M MALHOTRA[2], A PATTEN[3], LY NGO[2]
[1]Meridian Clinical Research, LLC, Savannah, GA, USA; [2]Eisai Inc., Woodcliff Lake, NJ, USA; [3]Eisai Ltd., Hatfield, Hertfordshire, UK

Objective: Perampanel is a once-daily oral anti-seizure medication (ASM) for POS and PGTCS. Study 311 (NCT02849626) was a multicentre, open-label, single-arm study of perampanel oral suspension in paediatric patients (aged 4–<12 years) with POS (with/without secondarily generalised seizures [SGS]) or PGTCS. Here, we report efficacy/safety of adjunctive perampanel 4mg/day in paediatric patients (aged 4–<12 years) with POS (with/without SGS) or PGTCS in Study 311.
Methods: The Core Study comprised 4-week Pretreatment, 23-week Treatment (11-week Titration; 12-week Maintenance), and 4-week follow-up periods. Efficacy assessments included median percent reductions in seizure frequency per 28 days from baseline during the Treatment Period, and 50% responder and seizure-freedom rates during Maintenance in patients receiving a modal (most frequent) perampanel dose of 4mg/day. Treatment-emergent adverse events (TEAEs) were assessed in patients receiving perampanel 4mg/day at onset of their TEAE(s).
Results: Overall, 30 patients received perampanel 4mg/day (modal dose; POS: n=24; SGS: n=10; PGTCS: n=6). Median percent reductions in seizure frequency per 28 days for POS, SGS and PGTCS were 34.2%, 36.6% and 100.0%, respectively. Fifty-percent responder rates for POS, SGS and PGTCS were 10/24 (41.7%), 5/10 (50.0%) and 3/4 (75.0%), respectively. Seizure-freedom rates for POS, SGS and PGTCS were 3/24 (12.5%), 2/10 (20.0%) and 3/4 (75.0%), respectively. TEAEs occurred in 60/145 (41.4%), 26/52 (50.0%) and 14/31 (45.2%) patients with POS, SGS and PGTCS, respectively, who were receiving perampanel 4mg/day at onset of their TEAE(s). The most common TEAE in patients with POS and SGS was nasopharyngitis (6.2% and 11.5%); dizziness, irritability and pyrexia were the most common in patients with PGTCS (9.7% each).
Conclusions: These data suggest adjunctive perampanel 4mg/day is an effective and well tolerated ASM for paediatric patients (aged 4–<12 years) with POS (with/without SGS) or PGTCS.

Poster No. 169

Time to onset of Cannabidiol (CBD) treatment effect and resolution of adverse events in the tuberous sclerosis complex Phase 3 randomised controlled trial (GWPCARE6)

H COCK[1], JY WU[2], O DEVINSKY[3], C JOSHI[4], I MILLER[5], CM ROBERTS[6], R SANCHEZ-CARPINTERO[7], D CHECKETTS[8], F SAHEBKAR[9]

[1]St. George's University of London, St. George's University Hospitals NHS Foundation Trust, London, UK; [2]UCLA Mattel Children's Hospital, Los Angeles, CA, USA; [3]NYU Comprehensive Epilepsy Center, New York, NY, USA; [4]Children's Hospital Colorado, Aurora, CO, USA; [5]Nicklaus Children's Hospital, Miami, FL, USA; [6]Oregon Health & Science University, Portland, OR, USA; [7]Clínica Universitaria de Navarra, Pamplona, Spain; [8]GW Research Ltd, Cambridge, UK; [9]Greenwich Biosciences, Inc., Carlsbad, CA, USA

Objective: Add-on cannabidiol (CBD) significantly reduced seizures associated with tuberous sclerosis complex (TSC) across the 16-week double-blind treatment period in GWPCARE6 (NCT02544763). A post hoc analysis was conducted to estimate time to onset of CBD treatment effect and resolution of adverse events (AEs).

Methods: Patients received GW Pharmaceuticals' formulation of plant-derived highly purified CBD (100 mg/mL oral solution) at 25mg/kg/day (CBD25) or 50mg/kg/day (CBD50), or placebo for 16 weeks. Treatment started at 5mg/kg/day for all groups, reaching 25mg/kg/day on Day 9 in CBD25 and 50mg/kg/day on Day 29 in CBD50. Percentage change from baseline in primary endpoint TSC-associated seizures (countable focal or generalised) was calculated by cumulative day (i.e., including previous days). Time to onset and resolution of AEs were evaluated.

Results: Overall 224 patients were randomised 1:1:1 to CBD25 (n=75), CBD50 (n=73), and placebo (n=76). The median (range) age was 11 (1–57) years. Patients had discontinued a median of 4 antiepileptic drugs (AEDs) and were currently taking a median of 3 AEDs. Differences in seizure reduction between CBD and placebo emerged on Day 6 (when titration reached 15mg/kg/day) and became nominally significant ($p<0.05$) by Day 11 (CBD50) or Day 12 (CBD25). Over 90% of patients had an AE, with onset during the first 2 weeks of the titration period in 63%. AEs resolved within 4 weeks of onset in 42% of placebo and 27% of CBD patients and by end of study in 78% of placebo and 51% of CBD patients; most frequent AEs—diarrhoea, somnolence, decreased appetite—resolved in 69–88% of CBD patients.

Conclusions: Findings suggest that onset of treatment effect (efficacy and AEs) occurred within the first 2 weeks. AEs lasted longer for CBD vs. placebo but resolved within the 16-week study in most patients.

Poster No. 170

Outcome following epilepsy surgery in patients with Tuberous Sclerosis: Experience from a single centre in the UK

L SINGH[1], M CHIPAUX[4], S FERRAND-SORBETS[4], F D'ARCO[5], A CHARI[2,3], JH CROSS[1,2], F O'CALLAGHAN[1,2], M TISDALL[2,3], C ELTZE[1]

[1]Paediatric Neurology Department, Great Ormond Street Hospital for Children, London, UK; [2]Developmental Neurosciences, Great Ormond Street Institute of Child Health, University College London, London, UK; [3]Department of Neurosurgery, UCL Great Ormond Street Institute of Child Health, London, UK; [4]Pediatric Neurosurgery Unit, Rothschild Foundation Hospital, Paris, France; [5]Department Neuroradiology, Great Ormond Street Hospital for Children, London, UK

Objective: Epilepsy surgery (ES) benefits some children with tuberous sclerosis (TS) and refractory epilepsy (RE). We report seizure outcomes of children with TS following ES at our institution and investigate predictive factors.

Methods: All children with TS, who underwent ES at our institution were identified from the surgical data-base (2000–2019). We reviewed electronic records, pre- and post-op MRI's. We used Fisher-exact-tests to analyse relationships of categorical variables to outcomes (significance level $p<0.05$) and Mann Whitney U to compare means.

Results: 36 children were identified, postoperative outcomes available for 35 (17 females, mean age seizure-onset: 5.7 [SD $\pm$ 6.9] months, mean age at ES: 6.2 [SD+/- 4] years). Pre- and post-op MR images were evaluated for 27/36 (75%). Preoperatively 10/32 (31%) were diagnosed with Autism, 14/32 (44%) had moderate/severe cognitive impairment, 30/35 (86%) daily seizures 31/36 (86%), 27/36 (75%) multiple seizure types, 19 (53%) epileptic spams and 29/36 (80%) localising/lateraling semiology. A "largest hemispheric" tuber was identified on pre-op MRI in 25/27 (86%; median size: 27mm). Twenty patients (55%) underwent intracranial EEG (stereo-EEG:10; subdural-grids: 10). Most underwent tuber-resections (31/36, 86%) and 4 temporal lobectomies. After a median follow up of 2.5 years (range 0.5–16.9y, IQR 3.9) 18/35 (51%) had a favourable outcome (Engel I/II). Two patients had undergone a second surgery. Considering small sample-numbers no statistically significant relationship between favourable postsurgical outcome (Engel I/II vs Engel III/IV) and 'multiple vs single seizure type', 'stable seizure-semiology >12 vs < 12months pre-op', 'post-op MRI concordance - resection with largest hemispheric tuber and/or calcification' was found. Age at surgery was not significantly different between Engel I/II and less favourable Engel III/IV outcome groups.

Conclusion: Appropriately selected TS patients benefit from epilepsy surgery and a referral should be considered for those with refractory seizures.

Poster No. 171

Success of single-photon emission computed tomography in epilepsy surgery evaluation

S HABERMANN, C WILKINSON, K ST PIER, S PUJAR, C ELTZE

Great Ormond Street Hospital, London, UK

Objective: Epilepsy surgery can be an option for patients with pharmacoresistant epilepsy and can be curative. Pre surgical evaluation can be resource-intense and includes multi-modal

assessments including functional neuroimaging to help identify the location and extent of the epileptogenic zone. Single-photon emission computed tomography (SPECT) can provide useful information in localising the epileptogenic zone, but requires timely injection of the tracer and for the seizure to occur within the allocated time window. This study analysed SPECT success rates at a paediatric tertiary neurology centre.
Methods: Data from 50 patients who had a SPECT attempted during 2013 to 2019 was retrospectively analysed in terms of demographics, SPECT success and factors possibly influencing SPECT success.
Results: Of the 50 patients, SPECT was successful in 22 (44%). The most common reason for failure was no seizures occurring during the scanning window (21/28, 75%). Less frequent causes were isotope administered too late, child not cooperative for the scan, isotope not being available, seizure being too short and poor scan quality. There was no significant difference in SPECT success rate between patients who had seizures when awake (8/16, 50%), from sleep (7/17, 41%) or seizures from awake and sleep (7/17, 41%) (p=0.84). Likewise, the success rate was similar for seizures lasting less than 1 minute (6/13, 46%) and seizure duration of >1 minute (16/37, 43%) (p=0.86). SPECT was more likely to be successful in children who had 5 or more seizures daily (9/16, 56%), however there was no statistically significant difference compared to those with less frequent seizures (p=0.30).
Conclusion: SPECT is a resource-intensive investigation and the high failure rate in this audit highlight the importance of careful patient selection to maximise the benefit of this service.

Poster No. 172
Clinical characteristics and post-surgery seizure outcomes in children with hemimegalencephaly spectrum

E TALMON L ARMÉE[3,4], A MCLELLAN[1], S PUJAR[3], Z TAHIR[3], M TISDALL[3], W HARKNESS[3], R GUERRINI[2], JH CROSS[3]
[1]Royal Hospital for Sick Children, Edinburgh, UK; [2]Meyer Children Hospital of Florence, Florence, Italy; [3]Great Ormond Street Hospital for Children, London, UK; [4]Sozialpädiatrisches Zentrum Frankfurt Mitte, Frankfurt, Germany

Aim: To describe the clinical characteristics and seizure outcomes in children with hemimegalencephaly spectrum.
Methods: Retrospective case note review of children with a diagnosis of hemimegalencephaly spectrum reviewed between January 1990 and December 2008 at Great Ormond Street Hospital for Children. We collected patient demographics, clinical details, whether or not they had surgery, type of surgery and the post-surgical outcome at the last follow up.
Results: Complete clinical data with a minimum post-op follow up of 6 months was available on 58 children at the time of review. 38/58 (66%) were male. Associated syndromes were diagnosed in 9 (5.5%) children; epidermal naevus (3), linear sebaceous naevus (2), limb hypertrophy (2), and capillary haemangioma of limb (2). Median age at seizure onset was days; 37/58 (64%) had their seizure onset in the neonatal period. The left hemisphere was affected in 28 (48%). 43/58 (74%) patients underwent surgery, of whom 37 had a hemispherotomy or a hemispherectomy, and 6 had a less extensive focal resection or disconnection. (26%) children underwent more than one surgical procedure. Median age at first surgical procedure was 5 months. Median post-surgical follow-up was 5 years. The seizure outcomes at last follow up were, Engel class I in 23 (53.5%), Engel class II in 6 (4%), Engel class III in 2 (28%) and Engel class IV in 2 (4.5%).
Conclusion: In this large series of patients with hemimegalencephaly spectrum, the majority had a good seizure outcome (Engel class I or II) following epilepsy surgery.

Poster No. 173
Surgical management of pediatric patients with pharmacoresistant epilepsy: comparison of pre-operative MRI and neuropathologic findings

J SZELEWICKI[1], B SINCLAIR[2,3], N LIU[2,3], A TAMM[4], J KASSIRI[2,3]
[1]University of Alberta, Edmonton, Canada; [2]Department of Pediatrics, University of Alberta, Edmonton, Canada; [3]Comprehensive Epilepsy Program, Stollery Children's Hospital, Edmonton, Canada; [4]Department of Radiology and Diagnostic Imaging, University of Alberta, Edmonton, Canada

Objectives: Poorly controlled seizures in childhood have a detrimental impact on the developing brain. In children with refractory epilepsy, surgical resection of epileptogenic foci can be an effective means of achieving seizure control. Neuroimaging is crucial to accurately localize epileptogenic foci and influences pre-surgical patient counselling and post-surgical seizure control. The objective of our study is to compare pediatric epilepsy surgery patients' pre-surgical MRI (either 1.5 or 3 Tesla (T) magnet strengths) findings with post-surgical neuropathology results and post-surgical seizure outcome.
Methods: Retrospective chart review was performed on 62 pediatric patients enrolled in the Comprehensive Epilepsy Program at the University of Alberta Hospital between January 1, 2015 to April 30, 2020; 25 met inclusion criteria. Data including patient demographics, pre-surgical MRI findings, tissue pathology results, and post-surgical seizure outcome at 12 months were collected from electronic medical records, entered into REDCap database, and analyzed. Concordance was defined as complete, partial (correct category of neuropathology identified or correct diagnosis on a list of ≥ 2 differential diagnoses on MRI report), or no concordance.
Results: Complete, partial and no concordance were observed in 12/25 (48%), 7/25 (28%), and 6/25 (24%) patients, respectively. Excluding patients with focal cortical dysplasia (FCD), complete, partial and no concordance were observed in 10/19 (52.6%), 7/19 (36.8%), and 2/19 (10.5%) patients, respectively. 13 of the original 25 patient cohort currently have post-operative follow-up data available at 12 months. Of these, 11 patients (84.6%) with partial or complete concordance were seizure-free.
Conclusions: These data demonstrate that MRI can accurately identify pre-surgical lesions in most refractory epilepsy patients, with the exception of patients with FCD. Exclusive use of higher resolution 3T MRI to identify epileptogenic foci should improve likelihood of accurate lesion identification and radiologic-neuropathologic concordance, optimizing surgical outcomes.

Poster No. 174

The perceived impact of COVID-19 and associated restrictions on young people with epilepsy in the UK: young people and parent survey

C REILLY[1,2], A MUGGERIDGE[1], J H CROSS[1,2,3]
[1]Research Department, Young Epilepsy, Lingfield, UK; [2]UCL Great Ormond Street Institute of Child Health, London, UK; [3]Great Ormond Street Hospital for Children NHS Trust, London, UK

Objective: To garner the views and experiences of young people with epilepsy and caregivers regarding the impact of the COVID-19 pandemic and subsequent restrictions in the UK.
Methods: An online survey was used to explore the views of young people (n=71) with epilepsy and caregivers (n=127) between 4th and 28th June 2020. It included sections on the impact of the COVID-19 pandemic and associated restrictions on the child's epilepsy and on child and caregiver wellbeing.
Results: One in 3 young people and one in four caregivers reported that the young person's seizures had increased during lockdown; only 7% of parents and 10% of young people reported a decrease. Half of young people reported that they were more reluctant to go to hospital for appointments. The majority of young people reported their sleep (73%), mood (64%) and levels of physical activity (53%) had deteriorated. However, 46% reported there had been positive aspects to the restrictions (eg, spending more time with family). 19% of parents reported difficulties getting their child's medication whilst 25% reported their child had clinical procedures/investigations (such as EEG/MRI/-surgery) cancelled during restrictions. Caregivers reported that their child's mood (60%), sleep (65%) and behaviour (50%) had deteriorated during the restrictions. The majority of caregivers experienced increases in stress (70%) anxiety (66%) and difficulties with sleep (58%). Epilepsy nurses, online support groups/charity websites were seen as the most helpful supports for both young people and parents/carers during the restrictions.
Conclusions: Survey results indicate that the pandemic and associated restrictions have had a negative impact on young people with epilepsy. Perceived increases in seizures and reluctance to go to hospital are likely to impact on epilepsy management. The wider psychosocial impact is also likely to be significant with increases in child and parent mental health problems in an already vulnerable group.

Poster No. 175

PROVE study 506: Retrospective, phase IV study of Perampanel in real-world clinical care of patients aged 4–<12 years with epilepsy

M CHEZ[1], A PATTEN[2], M MALHOTRA[3]
[1]Sutter Health, Roseville, CA, USA; [2]Eisai Ltd., Hatfield, Hertfordshire, UK; [3]Eisai Inc., Woodcliff Lake, NJ, USA

Objective: There are limited data on real-world use of perampanel, a once-daily oral anti-seizure medication for partial-onset seizures and primary generalised tonic-clonic seizures, in paediatric patients in the US. Here, we report retention rates, safety and efficacy of perampanel administered to paediatric patients (aged 4–<12 years) with epilepsy during routine clinical care from PROVE (NCT03208660).
Methods: Data were obtained from records of patients who initiated perampanel treatment after 1 January 2014. Follow-up was completed on 15 March 2019. The primary endpoint was retention rate (proportion of patients in the Safety Analysis Set [SAS] remaining on perampanel at 3, 6, 12, 18 and 24 months following treatment initiation). Safety, efficacy and dosing experience were secondary *Objectives:*.
Results: SAS included 203 patients aged 4–<12 years (mean [standard deviation] {SD} age: 8.2 [2.3] years; 51.7% female). Perampanel dose was titrated: weekly (20.7% of patients), every 2 weeks (21.2%), every 3 weeks (3.0%) and 'other' (55.2%). Mean (SD, range) maximum perampanel dose was 5.3 (2.9, 0–16) mg/day; mean (SD, range) cumulative duration of exposure to perampanel was 15.1 (13.6, 0.0–58.1) months. At data collection, 100 (49.3%) patients were ongoing on perampanel; 98 (48.3%) had discontinued. Primary reasons for discontinuing included adverse events (n=39 [19.2%]) and inadequate therapeutic effect (n=33 [16.3%]). Retention rate on perampanel at 24 months was 42.0% (n=47/112). Treatment-emergent adverse events (TEAEs) occurred in 64 (31.5%) patients; aggression (6.9%), somnolence (3.9%) and seizure (3.4%) were most common. Twenty-six patients had TEAEs of mixed psychiatric symptoms leading to discontinuation. Serious TEAEs occurred in 6 (3.0%) patients.
Conclusions: This analysis of PROVE suggests daily oral doses of perampanel are generally well tolerated with favourable retention rates for up to 2 years in paediatric patients (4–<12 years) with epilepsy treated during routine clinical care.

Poster No. 176

Our experience of Brivaracetam, a newer antiepileptic drug (AED), in the treatment of children with difficult to manage epilepsy – A 4-year retrospective, single quaternary centre study

SC CHELLADURAI, RG GUPTA
Birmingham Children's Hospital, Birmingham, UK

Objective: To determine the efficacy, side effects and retention rates of Brivaracetam in children with refractory epilepsy at our hospital.
Methods: Retrospective data was collected from clinical letters and pharmacy records for n=23 children treated with Brivaracetam in the past 4 years. Data included demographics, seizure types, previous AEDs, other treatments, dosage, side effects, efficacy, and duration. n=1 was omitted due to insufficient data.
Results: Demographics: n=22, Age range: 6 to 18 years, mean 12.5 years, median 12.6 years. Primary seizure type/syndrome: (n=22) n=6 generalised tonic-clonic, n=4 tonic spasms, n=1 atonic, n=2 myoclonic, n=2 absence, n=4 focal, n=1 Juvenile Myoclonic epilepsy, n=1 Familial dysautonomia, n=1 Lennox Gastaut Syndrome. Prior treatments: Number of AEDs=4.7 (range 1–10, mean 4.7, median 3.5); Epilepsy surgery pathway n=14 (63.5%), resective surgery n=2 (9%), VNS n=10 (45.5%), ketogenic diet n=9(41%); Maximum Brivaracetam dosage (mg/kg/day): n=3 (13.5%) ≤1, n=10 (45.5%) 2 to 3, n=7 (32%) 4–5, n=2 (9%) 7–8. Side effects: n=7 (32%) patients displayed side effects; n=4 (18%) behavioural, n=2 (9%) lethargy/low mood, n=1 (4.5%) sleeping difficulty; Medication stopped in n=12 (54.5%); Reason: poor control/no response in n=6 (27%), poor control with side effects in n=5 (23%), behavioural difficulties in n=1 (4.5%). Impact on

seizures: n=2 (9%) increased seizures. n=9 (41%) no effect; n=9 (41%) seizure improvement, of which n=3 (13.5%) <50% improvement, n=4 (18%) ≥50% improvement, n=2 (9%) 100% seizure suppression; n=2 (9%) unclear. Treatment duration: n=3 (13.5%) <3 months; n=7 (32%) 3 to 6 months; n=7 (32%) 7 to 12 months; n=4 (18%) 13 to 24 months; n=1 (4.5%) 44 months.
Conclusions: Brivaracetam is an effective AED for some children with intractable epilepsy. Potential side effects include behavioural problems, lethargy, difficulty in sleeping and increased seizures. Most patients continued Brivaracetam beyond 3 months. Further studies are necessary to better determine its efficacy and optimal dosing regimes.

Poster No. 177
Impact of COVID-19 on paediatric epilepsy services and what learning points can be taken forward for the future

ZK KHAN[1], RB BROWN[2,3]
[1]School of Clinical Medicine, University of Cambridge, UK; [2]Addenbrooke's Hospital, Cambridge, UK; [3]OPEN UK

Objective: To investigate the impact COVID-19 has had on children's epilepsy services and what learning points can be taken forward for the future.
Methods: Emails were sent out to all members of the Eastern Paediatric Epilepsy Network (EPEN), a network of clinicians delivering paediatric epilepsy care in the east of England. Members were asked to offer their perspective on how COVID-19 has affected the epilepsy service they provide, and what improvements could be taken forward for the future. Qualitative data was collected from 25 respondents, representing all (100%) of the 16 units across the region.
Results: There was a shift from face-to-face patient consultations to telephone/video call. On the whole this was very positively received by both families and staff. Negatives brought up included issues surrounding safeguarding and difficult communication. There was a big drop in numbers of patients arriving to ED. A significant number of inappropriate attendances in ED were avoided, but there were examples of delayed presentations of children with severe disorders. Several epilepsy specialist nursing teams struggled with the increased workload of dealing with families of complex patients who were not coping well with cancellation of schools/clubs/CAMHS etc. Neurophysiology and imaging services were initially closed. On re-opening, many patients 'shielding' were reluctant to come to hospital. MDT meetings and teaching utilised videoconference platforms. This was well received with greater turnouts than pre-COVID-19. Registrar training opportunities were reduced. Looking into the future, responses foresaw a mixture of face-to-face and virtual consultations, and using virtual platforms for MDT meetings and teaching.
Conclusions: COVID-19 has had both positive and negative impact on children's epilepsy services. In the future, undertaking clinical assessment, teaching, and multi-disciplinary work through use of remote technology will be the predominant benefits.

Poster No. 178
Long-term (1-year) seizure freedom with adjunctive Perampanel in paediatric patients (aged 4–<12 years) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS): post hoc analysis of study 311

R FLAMINI[1], A PATTEN[2], M MALHOTRA[4], LY NGO[3]
[1]Pediatric and Adolescent Neurodevelopmental Associates, Atlanta, GA, USA; [2]Eisai Ltd., Hatfield, Hertfordshire, UK; [3]Eisai Inc., Woodcliff Lake, NJ, USA; [4]Eisai Inc., Woodcliff Lake, NJ, USA

Objective: Perampanel is a once-daily oral anti-seizure medication (ASM) for POS and PGTCS. Long-term seizure-freedom rates with adjunctive perampanel are maintained in adolescents/adults (aged ≥12 years) with secondarily generalised seizures (SGS) or PGTCS. We assessed if seizure-freedom rates with adjunctive perampanel during the 311 Core Study (NCT02849626) are maintained during long-term treatment in paediatric patients with POS (with/without SGS) or PGTCS.
Methods: Seizure-freedom rates (POS, SGS, PGTCS) were assessed in patients who achieved seizure freedom during the Core Study Maintenance Period and then remained seizure free for 6 and/or 12 months (calculated from the start of their seizure-free period). Data were stratified by concomitant enzyme-inducing ASMs (EIASMs) (with/without) and age (4–<7/7–<12 years).
Results: For POS, 13/17 (76.5%) seizure-free patients during the Core Study remained seizure free for 6 months (with EIASMs, n=3/5 [60.0%]; without EIASMs, n=10/12 [83.3%]; 4–<7 years, n=1/3 [33.3%]; 7–<12 years, n=12/14 [85.7%]), and 6/11 (54.5%) remained seizure free for 12 months (with EIASMs, n=2/5 [40.0%]; without EIASMs, n=4/6 [66.7%]; 4–<7 years, n=0/1; 7–<12 years, n=6/10 [60.0%]). For SGS, 3/8 (37.5%) seizure-free patients remained seizure free for 6 months (with EIASMs, n=0/1; without EIASMs, n=3/7 [42.9%]; 4–<7 years, n=0/3; 7–<12 years, n=3/5 [60.0%]), and 1/5 (20.0%) patients remained seizure free for 12 months (with EIASMs, n=0/1; without EIASMs, n=1/4 [25.0%]; 4–<7 years, n=0/2; 7–<12 years, n=1/3 [33.3%]). For PGTCS, 6/10 (60.0%) seizure-free patients remained seizure free for 6 months (no PGTCS seizure-free patients received EIASMs; 4–<7 years, n=1/2 [50.0%]; 7–<12 years, n=5/8 [62.5%]), and 3/7 (42.9%) patients remained seizure free for 12 months (4–<7 years, n=0/1; 7–<12 years, n=3/6 [50.0%]).
Conclusions: Despite small patient numbers, seizure-freedom rates are maintained during long-term perampanel treatment in paediatric patients, consistent with analyses in adolescents/adults.

Poster No. 179
Epidemiology and outcome of status epilepticus in children with new ILAE definition – Scottish population cohort

C MITCHELL[1,2], L DICKSON[1], A RAMSAY[1], O MESALLES-NARANJO[3], P LEONARD[4], C BRAND[4], A MCLELLAN[4], J SHETTY[4]
[1]University of Edinburgh Medical School, Edinburgh, UK; [2] Freeman Hospital, Newcastle upon Tyne, UK; [3]Merkle Inc, Bermondsey, London, UK; [4]NHS Lothian, Edinburgh, UK

Objective: Status Epilepticus (SE) in children carries significant risk of morbidity and mortality. Previous work has predominantly

focused on SE ≥30 minutes but the new ILAE definition classifies SE ≥ five minutes. This study aims to evaluate the epidemiology and outcome of SE since the introduction of buccal midazolam, change in ILAE definition and increased involvement of specialist epilepsy nurses.

Methods: Multiple datasets were combined to identify all children presenting to paediatric emergency departments (ED) between 2011-2017 in Lothian, Scotland. Data, collated from electronic health records, included patient demographics, clinical characteristics, acute seizure management and outcomes.

Results: There were 665 children admitted with SE who had 1228 seizure episodes during the study period. SE accounted for 0.38% (95% CI 0.34–0.42%) of annual ED attendances. Yearly prevalence was 0.8 per 1000 children. 57.3% of patients were male (95% CI 53.5–61.1%) and median age was 3.65 years (IQR=6.33, Min=0.0, Max=20.97). The median number of SE for each child was 1, however, 34.1% of children had recurrent SE and 5.6% had ≥5 SE. Median seizure duration was 10 min. 30.3% of seizures lasted between 5 to 29 min. Recurrent seizures and longer duration both increased odds of adverse outcome. Buccal midazolam was used in the management of 28.9% of seizures and had no effect on the need for ventilatory support. 69.8% SE required hospital admission and only 4.0% resulted in adverse outcome. Of 1228 seizure episodes, there were 2 deaths (0.2%). Compared to symptomatic seizures, unprovoked seizures had a greater average duration and likelihood of adverse outcomes.

Conclusions: Adverse outcomes have decreased and the use of buccal midazolam is promising. Identifying high-risk groups provides opportunity for early intervention. This data forms the basis for extensive evaluation of acute seizure management and monitoring long-term outcomes.

Poster No. 180

Preliminary pharmacokinetic (PK) and safety data of adjunctive Perampanel oral suspension in paediatric patients (aged >6 to <24 months) with epilepsy in Study 238

M ZAFAR[1], G ROZENTALS[2], JB RENFROE[3], J ALURI[4], D KUMAR[4], LY NGO[4]

[1]Duke University, Durham, NC, USA; [2]Children's Clinical University Hospital, Riga, Latvia; [3]Child Neurology Center of Northwest Florida, Gulf Breeze, FL, USA; [4]Eisai Inc., Woodcliff Lake, NJ, USA

Objective: Perampanel is a once-daily oral anti-seizure medication (ASM) for partial-onset seizures and primary generalised tonic-clonic seizures. ASM selection for patients aged <4 years can be difficult due to a lack of clinical studies in this population. We report preliminary PK and safety/tolerability data from Study 238 (NCT02914314), the first study evaluating adjunctive perampanel in patients aged ≥1–<24 months with epilepsy.

Methods: Study 238 is a multicentre, open-label, Phase II study comprising 2-week Pretreatment and up to 20-week Treatment Phases (Core Study), and a 32 to 36-week Extension Phase. Planned enrollment is ≥16 patients with evaluable PK data. Perampanel is initiated at 0.5mg/day and titrated to a maximum of 12mg/day (without enzyme-inducing ASMs [EIASMs]) or 16mg/day (with EIASMs) based on clinical response and tolerability. Endpoints include plasma perampanel levels during the Core Study Maintenance Period and safety (e.g. treatment-emergent adverse events [TEAEs], laboratory tests, vital signs and electrocardiogram).

Results: As of 27 January 2020, perampanel treatment was administered to 12 patients (aged >6–<24 months). Nine patients completed the Core Study, 2 are ongoing and 1 discontinued early (inadequate therapeutic effect). All patients who completed the Core Study entered the Extension Phase; 7 patients completed the Extension and 2 discontinued (patient choice). Plasma concentrations from the patients (8 without and 1 with an EIASM) with available PK data suggest perampanel exposure is within the range observed in patients aged ≥2 years. Eleven (91.7%) patients had TEAEs; most common was upper respiratory tract infection. Five (41.7%) patients had unrelated, serious TEAEs. No patients experienced worsening of generalised seizures.

Conclusions: Preliminary data suggest perampanel is well tolerated in patients aged >6–<24 months. Perampanel exposure is within the range observed in patients aged ≥2 years; the safety profile is consistent with prior studies. Enrollment is ongoing.

Poster No. 181

Fenfluramine reduces seizure burden by significantly increasing number of seizure-free days and time between seizures In patient with Dravet syndrome

JH CROSS[1], O DEVINSKY[2], B GALER[3], G FARFEL[3], A GAMMAITONI[3], JE SULLIVAN[4], A GIL-NAGEL[5], S AUVIN[6]

[1]UCL Great Ormond Street Institute of Child Health, Great Ormond Street Hospital, London, UK; [2]NYU Langone Medical Center, New York, NY, USA; [3]Zogenix Inc., Emeryville, CA, USA; [4]University of California San Francisco, Benioff Children's Hospital, San Francisco, CA, USA; [5]Hospital Ruber Internacional, Madrid, Spain; [6]Robert Debré Children's Hospital, Paris, France

Objective: A recent clinical trial with 0.7mg/kg/day of fenfluramine (FFA) showed 62.3% (IC 95%: –47.7%; –72.8%; p<0.001) reduction in convulsive seizure frequency (CSF) compared to placebo. However, the impact of the disease on the patient and their caregivers may depend on other variables. This alternative analysis value the impact of other results.

Methods: After a baseline period of 6 weeks patients with DS ages 2 to 18 years, was randomized to FFA 0.7 or 0.2mg/kg/day or placebo added. Time to new event (time required to experience the same number of crisis as in the reference period [TTE]) was analyzed. Intervals without crisis and number of days without crisis was analyzed too.

Results: 119 patients with DS receiving FFA 0.7mg/kg/day; FFA0.2mg/kg/day; or placebo. TTE was significantly longer in active groups. Placebo: 6 weeks, FFA 0.2mg/kg/day:8 weeks and FFA 0.7mg/kg/day: >12 weeks (p<0.001; ~60% of patients in the FFA 0.7mg/kg/day group never reached their baseline seizure count and were censored). The number of days without crisis was higher in groups treated with FFA: 33 and 20 days without additional crisis counted in the active groups. The longest average without crisis was higher with FFA 0.7mg/kg/day (25 days; p<0.001) and FFA 0.2mg/kg/day (15 days; Px0.035) than with placebo (9.5 days).

Conclusion: FFA extended TTE and provided significantly more days without crisis and longer periods without crisis than placebo. Our analysis can help assess the ability of a treatment to reduce the burden of seizures in patients with SD and their caregivers.

Poster No. 182

"Maybe. . .don't scare them too much"; Exploring parental and clinician perceptions to build an understanding of the doctor-parent relationship in paediatric epilepsy

M GENTRY ESPINOSA[1], N SCHINDLER[2,3], M KALIAKATSOS [4], A SIVARAJAH[1], A HAMEED [1]

[1]Medical School, University College London, London, UK; [2]Department of Paediatrics, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, UK; [3]Institute of Continuing Education, University of Cambridge, Cambridge, UK; [4]Department of Paediatric Neurology, Great Ormond Street Hospital, London, UK

Objective: Trust and a healthy relationship between doctor and parents is associated with improved outcomes in children and young people with long term conditions, while communication difficulties are often cited as a central cause of complaints. This study aims to explore the perspectives and experiences of parents, carers and clinicians around the doctor-parent relationship in paediatric epilepsy services.
Methods: A literature search was performed to identify parental perceptions around the doctor-parent relationships in epilepsy care. Semi-structured interviews were conducted with clinicians working in paediatric epilepsy to explore their perspective of the same issues. Thematic analysis was used to identify themes within the interview data, which were compared with established themes within the literature.
Results: 18 relevant articles were identified and 5 clinicians were interviewed. (1) Both parents and clinicians recognised the value of patient-centred care, although clinicians felt reliant on parents being open about their concerns for these to be addressed. (2) Effective communication was recognised as a valuable contributor to a successful doctor-parent relationship by parents and clinicians, with both aware of how the other may act to facilitate or inhibit this. (3) Clinicians valued honesty and sharing of personal and clinical experiences as strategies to help build trust with parents. (4) Parents placed a greater emphasis on psychosocial support and the provision of information, while clinicians were concerned about overwhelming or scaring parents with too much information.
Conclusion: Parents and clinicians felt that trust, and communication skills were central to the doctor-parent relationship. Despite this commonality, parents and doctors may have differing ideas of how much information should be shared in a consultation, with a desire for more information competing with a concern about overwhelming the family. A focus on the ways in which these tensions can be navigated may help improve the doctor-parent relationship in epilepsy services.

Poster No. 183

Is there a surgical hypothesis? KCNQ2 genetic encephalopathy presenting as a mimic of an early onset structural focal epilepsy

A PARIDA[1,2], R KUMAR[2], E WASSMER[2], R ALI[2], S AGRAWAL[2]

[1]Department of Paediatric Neurology, Oxford Children's Hospital, Oxford, UK; [2]Department of Paediatric Neurology, Birmingham Children's Hospital, Birmingham, UK

Introduction: We describe two cases of early onset drug resistant epilepsy with concordant seizure semiology, MRI and EEG abnormalities to support a likely structural focal aetiology. In both cases a pathogenic variant of the KCNQ2 gene was found.
Methods: Retrospective case notes review.
Results: Case 1- A baby born at term in good condition developed recurrent tonic seizures from 90 minutes of life. Semiology was characterised by stereotypical left sided tonic stiffening at onset corresponded with seven captured right hemispheric seizures on EEG. Imaging showed diffuse blurring of the grey-white matter junction in the right hemisphere with concordant PET abnormalities showing reduced tracer uptake throughout the right hemisphere. Seizures were drug resistant. Mild early developmental impairment was present. At 6 months of age a surgical proposal of a right hemispherotomy was made. Subsequently, a de novo heterozygote pathogenic variant of KCNQ2c.740C>T p.(scr247leu) was found so hemispherotomy did not proceed. Case 2- An infant of non-related parents born at term presented at 4 months of age with stereotyped seizures with forced deviation of the eyes and neck to the right side at onset. EEG showed left frontal interictal epileptiform activity concordant with MRI brain showing an area of possible focal cortical dysplasia in the left frontal lobe. Seizures were drug resistant and mild early developmental impairment was observed. Epilepsy Surgery work-up was initiated but was halted when a likely pathogenic heterozygote variant of KCNQ2c.1955dup.p.(Thr653Aspfs*212) was identified.
Discussion: These cases demonstrate the expanding spectrum of KCNQ2 related epilepsy and how it may have similar neuroimaging and electroclinical features to epilepsies caused by a cortical dysplasia. We suggest having a low threshold for considering a next generation epilepsy gene panel in all cases of drug resistant early onset epilepsy even when a structural abnormality is being strongly suspected.

Poster No. 184

Which cortical tuber type is more epileptogenic? Magnetic resonance imaging-based study in children with tuberous sclerosis complex

AA EL-BEHEIRY[1], HM NASSEF[1], RM DARWISH[1], TEI OMAR[2], HM HUSSEIN[2]

[1]Department of Radiodiagnosis, Faculty of Medicine, University of Alexandria, Alexandria, Egypt; [2]Department of Paediatrics, Faculty of Medicine, University of Alexandria, Alexandria, Egypt

Background: Cortical tubers are the most common brain lesions in patients with tuberous sclerosis complex (TSC). Relationship between cortical tubers and the severity of seizures is challenging and still not totally understood.

Objective: The aim was to identify different types of cortical tubers in children with TSC on the basis of MRI and to evaluate the relationship between these tuber types and severity of epilepsy.
Methods: Twenty children with a history of TSC and neurological manifestations, mainly epilepsy, were enrolled in this prospective study. All patients were examined by conventional MRI imaging including 3D T1, axial T2, axial fluid-attenuated inversion-recovery (FLAIR), diffusion-weighted imaging, and susceptibility weighted imaging. Characterization of different types of tubers was performed on the basis of the signal intensity of their subcortical white matter. Association between the severity of epilepsy and types of cortical tubers was studied.
Results: Four types of cortical tubers were identified labelled A, B, C, and D. Type A was only identified on T2 and FLAIR. Type B showed a hypointense T1 signal with hyperintensity on T2 and FLAIR. Type C was cystic, with the highest apparent diffusion coefficient values. Type D was calcified with blooming on susceptibility weighted imaging. Patients were grouped into 4 groups according to the tuber types. There was a significant difference between different groups and frequency of seizures ($p<0.05$). Group A showed the most favourable course, whereas groups C and D showed a higher association with more severe phenotypes.
Conclusions: Cortical tubers can be classified into different types on the basis of their MRI signal intensities. Identification of these types is a valuable non-invasive diagnostic measurement in the assessment of the severity of seizures in TSC patients, which may help in tailoring the treatment for each patient.

Poster No. 185
Supporting PREVENT for girls on Sodium Valproate with COVID-19 challenges

N GANJOO[2], J CHIA[2], M WAYLAND[1], M SMITH[2]
[1]Addenbrooke's Hospital, Cambridge, UK; [2]Peterborough City Hospital, Peterborough, UK

Objective: In March 2018, MHRA endorsed the view that sodium valproate should not be used in woman or girls in child bearing age unless she has PREVENT (pregnancy prevention programme) in place. With COVID-19 and additionally a recent gap in service in the paediatric epilepsy team, we wanted to firstly review the number of female patients on sodium valproate and then review implementation of pregnancy prevention programme (PPP).
Methods: Data was collected from 2019 audit and patient list from the epilepsy clinic. Lists were also requested from our paediatric pharmacists.
Results: 9 of 12 patients on previous lists were identified as being in child bearing age however following review only 4 continue on sodium valproate, 4 were switched and one weaned off her medication. 4 new patients were identified since last audit with initial documented discussion. In total, 8 girls required up-to-date Annual Risk Acknowledgement Form (ARAF), only 2 were completed.
Conclusion: The outstanding ARAF forms were a result of a temporary gap in service of a paediatric epilepsy lead compounded by cancellation of all outpatient activity due to COVID-19. However, following our review this has been urgently addressed by the team in line with adapted recommendations. There is temporary advice for management of annual review during COVID-19 suggesting communicating, if possible, the Valproate Patient guide and ARAF via email and paper forms by post to patients and families with documentation. Followed by review of ARAF at appointment. Subsequently confirmation of receipt of ARAF by patient can be via email/messaging service. Failure to receive response with patient agreement at 2 weeks needs chasing up. This has been presented at the 'Trust Audit Meeting' to share our experience of adapting services with COVID-19 considering a second wave of COVID-19 may lead to further cancellation of out patient activity.

Poster No. 186
Virtual clinics for paediatric epilepsy during the Covid-19 pandemic – is this a successful model for service delivery?

H HAMILTON[1,2], J BOTHWELL[2]
[1]Royal Belfast Hospital for Sick Children, Belfast, UK; [2]Belfast Health and Social Care Trust, Belfast, UK

Objectives: (1) To quantitatively review attendance at virtual epilepsy clinics during covid-19 in comparison with face-to-face clinics in the same period last year. (2) To qualitatively evaluate parent/carer opinion regarding the service delivery change.
Method: Retrospective study of virtual epilepsy clinic attendances were compared with face-to- face appointments. Electronic/paper records on attendance were reviewed for clinics completed March –August 2019 and 2020. A qualitative feedback survey with parent/carers was carried out by telephone in September 2020.
Results: Telephone virtual clinics improved the DNA rate by 37%. In 2019, 51 of 70 scheduled face-to-face reviews attended. 15 did not attend, and there were 4 cancellations, giving a DNA rate of 27%. During 2020 lockdown, 53 of 64 scheduled telephone reviews were completed. Eleven patients were uncontactable giving a non-attendance rate of 17%. Telephone clinics proved popular with patients due to less disruption to work and schoolwork, and a less stressful experience. 100% of parents felt that telephone review clinics were a good alternative to attending face-to-face clinic and their needs were sufficiently met via telephone. 40% of patients had reservations about a telephone-based service, as they found a face-to-face review more reassuring, had variable audio signal quality and the distraction of other children at home.
Conclusions: The classic model of consultant review at epilepsy clinic every 6-12 months is outdated in a modern society. Reforms to the review service of this relatively stable patient population are inevitable. Telephone clinics both improved attendance and had good feedback from the families. A blend of face-to-face and telephone reviews was the preferred option for families and would help provide an effective service, particularly in light of covid-19.

Poster No. 187
Infantile epilepsy caused by mutations in 2q24.3

KL STEVENSON, J PRICE, E HEYBURN, S TIRUPATHI
Royal Belfast Hospital for Sick Children, Belfast, UK

Objective: Inherited disorders of ion channel function are a rapidly expanding group of neurological disorders. The chromosome 2q24.3 region contains three genes encoding sodium channels (SCN1A, SCN2A, and SCN3A) and appears to play an important role in childhood epilepsy. The majority of deletions in the 2q24.3 region are associated with a severe epilepsy phenotype. Deletions in SCN1A are more commonly implicated in epilepsy

than SCN2A or SCN3A. Seizure onset is usually prior to 6 months of age. 2q24.3 Duplications are less well described with approximately 20 reported cases. These children present with severe neonatal seizures in the first days of life. However once seizure control is achieved these children often retain seizure freedom and have a relatively good outcome.
Methods: We report two cases of 2q24.3 duplication and one case of a deletion in the same region.
Results: One infant has a duplication affecting region containing SCN1A/2A/3A and achieved seizure control on phenobarbitone. At 10 weeks of age he was seizure free. The second child has a duplication of the region containing SCN2A/3A. He achieved control on phenytoin and zonisamide and was medication free at 3 years of age. The third patient with a large deletion involving SCN1A/2A/9A presented at 3 months of age with febrile status epilepticus. He is severely delayed, registered blind and has developed Lennox-Gastaut Syndrome. At age 4 years, he was seizure free for a month following the addition of CBD to stiripentol, clobazam and sodium valproate. At 5 years of age his seizure control remains poor.
Conclusions: The involvement of the SCN1A gene alongside SCN2A and SCN3A does not seem to affect prognosis in the case of duplication in the 2q24.3 region. However, deletions in the sodium channel cluster have a significant effect as demonstrated by the cases presented.

Poster No. 188
Myoclonic absence seizures in SETD1B-related neurodevelopmental disorder: an emerging phenotype

CM KEHOE[1], S O'CONNELL[2], HK ROBINSON[3], SA LYNCH[4], NM ALLEN[1]
[1]Department of Paediatrics (Neurology), National University of Ireland, Galway, Ireland; [2]Department of Neurophysiology, Galway University Hospital, Galway, Ireland; [3]Exeter Genomics Laboratory, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK; [4]Department of Clinical Genetics, Children's Health Ireland at Temple St. Children's Hospital and Our Lady's Children's Hospital, Dublin, Ireland

Epilepsy with myoclonic absences is a rare epilepsy syndrome characterised by absences with rhythmic myoclonic activity typically involving the shoulders and arms. Myoclonic absence seizures have been associated with several genetic disorders, including Angelman syndrome, GLUT1 deficiency syndrome and SCN1A/Dravet syndrome. In the majority however, no specific aetiology is determined. SETD1B encodes SET domain-containing protein-1B, a lysine-specific methyltransferase involved in histone methylation, modelling chromatin structure and gene transcription. SETD1B was recently associated with neurodevelopmental impairment and seizures. We describe a novel SETD1B variant in a boy with underlying epilepsy with myoclonic absences, and review the related literature. A 6.5-year-old boy, with intellectual disability and obesity, presented with myoclonic absence seizures. Physical examination was significant for increased BMI, dysmorphism (deep set eyes, short philtrum, dimpled chin and brachycephaly), and mild left gastrocnemius hypertonia. EEG showed bursts of generalised spike-wave with photosensitivity and captured a myoclonic absence seizure. MRI brain showed mild non-specific sub-cortical white matter abnormalities. Trio exome sequencing identified a novel de novo frameshift variant in SETD1B [c.22dup p.(His8Profs*30)]. Levetiracetam led to therapeutic response. Currently aged 7.5 years he suffers from intermittent challenging behaviour, but not autistic spectrum disorder. Literature review identified eight other cases of SETD1B-related disorder. All had idiopathic generalised epilepsy and three of also had myoclonic absence seizures. All had intellectual disability preceding onset and 6 had autism. SETD1B-related neurodevelopmental disorder adds further evidence for the role of deranged epigenetic processes (chromatin modelling) in the pathogenesis of epilepsy. In all cases to-date genetic generalised epilepsy presented in early childhood, and epilepsy with myoclonic absences in four of nine individuals. SETD1B-related neurodevelopmental disorder should be considered in patients presenting with myoclonic absence seizures as this gene is not on commercial epilepsy gene panels.

Poster No. 189
Novel homozygous CNTNAP2 mutation in two siblings with focal epilepsy and learning disabilities

JM PULLA, G VADLAMANI
Paediatric Neurology, Leeds Teaching Hospital, Leeds, UK

Background: Research implicates Contactin-associated protein-like 2 (CNTNAP2/CASPR2) gene in a wide spectrum of neurological disorders. Heterozygous mutations of this gene are frequent and associated with wide range of disorders such as autism, ADHD, Tourette syndrome, schizophrenia and can be present both in unaffected and affected individuals. Homozygous mutations in contrast, are rare and have been described to result in CASPR2 deficiency syndrome involving intellectual disability, epilepsy, language impairment, Autism and/or regression at seizure onset.
Clinical report: Two sisters from Pakistani consanguineous family presented with onset of symptoms of temporal lobe epilepsy between 2.5 and 3 years of age. By 6 years of age, they manifested significant learning difficulties, poor social abilities, aggressive behaviours and stereotypic hand flapping movements. In Sibling 2, epilepsy is more severe, and she has poor speech with no history of regression. Antenatal, birth and early developmental history are unremarkable. Parents and four other children are healthy. Sibling 1 has microcephaly and sibling 2 has a café au lait patch. Routine blood tests, metabolic investigations, CSF analysis and MRI brain are normal. EEG confirmed epileptic seizures of temporal lobe origin. Epilepsy gene panel testing, confirmed by Sanger sequencing, identified a missense variant of CNTNAP2 (NM_014141.6) c.682G>A p. (Gly228Arg), known to result in protein change G228R. This mutation is not previously described. Dysmorphism, MR abnormalities such as temporal cortical dysplasia, periventricular white matter abnormalities and language regression previously described in literature in cases with homozygous CNTNAP2 mutations are not present in our cases.
Conclusion: We report a novel homozygous mutation of CNTNAP2 gene, not been described previously, in two siblings with refractory temporal lobe epilepsy, learning difficulties, autistic traits, speech and language delay, but no developmental regression.

Poster No. 190

Experiences on the use of home video-telemetry in children during the COVID-19 pandemic: a family survey

L D'ARGENZIO[1], M SPARKLES[2], S TANG[1], Z AGIRRE[2], S GOYAL[2]

[1]Paediatric Neurology Department, Evelina Children's Hospital, London, UK; [2]Neurophysiology Department, Evelina Children's Hospital, London, UK

Background: Home video EEG-telemetry (HVT) is a well-established technique to reliably record seizures in children. HVT has two main advantages over inpatient video telemetry (IVT): is more cost-effective and allows children to stay at home during the recording. Furthermore, HVT has demonstrated to be as effective as IVT in capturing seizures/events of interest and provides excellent quality of the electroencephalographic recording. During the lockdown period of the recent COVID-19 pandemic, our department continued to perform HVT in children. Patients and their families were invited to attend the hospital for the setup and went home to complete the recording. A dedicated courier collected the equipment once the test was completed.

Objective: We aimed to survey families of children who underwent HVT during UK lockdown period in order to assess the feasibility of the technique during this period and gain feedback from service users.

Methods: Families were invited to fill anonymously a 20-question semi-structured interactive online survey. Descriptive analysis performed and selective constructive feedback was extrapolated and discussed with relevant stakeholders.

Results: After establishing a new pathway, 98 families were contacted and offered HVT since the starting of UK national lockdown. Of these, 18 declined to have the test – 17 for reasons related to COVID-19. 61/80 patients underwent HVT from March to June 2020. Of these, 17 families responded to the questionnaire. An overall satisfaction of 4.6/5 was reported. Parents felt safe to attend hospital during the pandemic in 82% of cases. 12/17 parents reported setup to be straightforward and 16/17 families found using of equipment at home easy or very easy, including the removal of the wires.

Conclusion: HVT has proved to be a safe procedure during the pandemic and its use should be considered as an alternative to IVT in children when hospital attendance not advisable for high-risk population.

Poster No. 191

Clinical features of children presenting with prolonged seizures - a data linkage study from a Scottish population cohort.

TS PELTZ, C MITCHELL, A RAMSAY, O MESALLES, A MCLELLAN, J SHETTY

Neurology, Royal Hospital for Sick Children, Edinburgh, Scotland, UK

Objective: Prolonged Seizures (PS), defined as seizures lasting over 5 minutes, are a common medical emergency that is not yet well correlated to clinical data. Here we aimed to study the correlation between PS, clinical features and investigation data (MRI, EEG and treatment details).

Methods: This study draws on an existing cohort of children who presented with PS to a tertiary children's hospital in Scotland between January 2011 and December 2017. We conducted a data linkage study using a unique identifier (CHI-number) for emergency admission data, neurology clinic records, the EEG database and MRI reports.

Results: There were 665 children with 1,234 presentations with PS. 57.30% of children were male. The median age was 3.65 years (IQR 6.33). 60.45% of admissions had a diagnosis of epilepsy, 24.40% were diagnosed before the PS and 75.60% after (61.88% were generalised seizures, 38.12% focal seizures). 55.67% had an EEG (30.28% normal, 40.47% abnormal and specific to epilepsy diagnosis, 29.26% abnormal but non-specific). 61.35% had an MRI scan (49.80% normal, 41.08% abnormal and associated with epilepsy, 7.40% abnormal and possibly related to epilepsy, 1.72% unrelated abnormal). 35.01% of patients were prescribed maintenance AED (43.35% polytherapy); the commonest AED was leviteracetam.

Conclusions: This large cohort allows a detailed analysis of the clinical features and aetiology of PS through data-linkage. Epilepsy diagnoses (previously known or subsequently diagnosed) are the commonest group with PS. Hence it is important to investigate children presenting with PS. In those investigated further, EEG and MRI abnormalities were specific to epilepsy. Of those prescribed AED, a large proportion were on polytherapy suggesting worse seizure control and PS. Overall, this serves as a valuable prognostic factor and aid in planning a clear emergency care plan for managing PS. We will be continuing to follow this cohort to study the clinical and educational outcomes.

Poster No. 192

RHOBTB2 de novo gene mutation and epileptic encephalopathy

M DUTTA[1], G AMBEGAONKAR[2], P AMATO GAUCI[3], M LEES[4], H DOLLING[5], L RAYMOND[6], A MENOUNOU[1], D KRISHNAKUMAR[2]

[1]Colchester Hospital, East Suffolk North Essex NHS Foundation Trust, Colchester, UK; [2]Child Development Centre Addenbrooke's Hospital, Cambridge University Hospitals NHS Trust, Cambridge, UK; [3]North West Anglia NHS Foundation Trust, UK; [4]Consultant, Clinical Geneticist, Great Ormond Street Hospital, London, UK; [5]School of Clinical Medicine, University of Cambridge, Cambridge Biomedical Campus, Cambridge, UK; [6]Cambridge University Hospitals NHS Foundation Trust, Cambridge Biomedical Campus, Cambridge, UK

Introduction: Mutations in RHOBTB2 have been shown to cause early onset epileptic encephalopathy and intellectual disability. We present two children with de novo RHOBTB2 mutations with missense variant c 1448G>A; p(Arg483His) in case 1 and c.1531C>T; p(Arg511Trp) in case 2,identified by Whole Genome Sequencing.

Case details: Both children were females, born at 34 weeks and term respectively, to non-consanguineous parents with normal early development. Case 1 had mild dysmorphism but case 2 was non dysmorphic. Case 1 Presented initially at 5 months with febrile status epilepticus and developed left focal epilepsy with secondary generalization. She has had three further afebrile status epilepticus. At age of 3 she has hypotonia, severe global developmental delay, movement disorder (dystonia and chorea) and controlled epilepsy on levetiracetam and sodium valproate. MRI brain shows mild generalised white matter volume loss and thin corpus callosum. Case 2 Presented at 4 months with right focal seizures related to fever, and subsequently developed recurrent, afebrile multi focal clonic seizures and three PICU admissions due to status. At age 9 months,

she also has global developmental delay, pharmaco-resistant epilepsy and is on ketogenic diet in addition to levetiracetam and carbamazepine. MRI brain reported as normal.
Discussion: The phenotype of both our cases is like those reported in literature. The common differential diagnosis of children with early onset febrile status usually includes SCN1A and PCDH19 related epilepsy. The RHOBTB 2 is increasingly described in the literature in children with early epileptic encephalopathy. Children (with/without dysmorphism) who present with recurrent afebrile seizures following initial febrile status and go on to have developmental delay, movement disorder, pharmaco-resistant epilepsy, and have non-specific abnormalities on MRI brain should be thoroughly investigated including Whole Genome Sequencing. For such cases we propose including RHOBTB2 gene in the Early Infantile Epileptic Encephalopathy panel.

Poster No. 193
Establishing an adolescence epilepsy transition clinic – An RCPCH EQIP project

D DEMETRIOU, M BARBER, J ANDERSON, C LAWTHOM, L CAPELING, J BARBER, K SPENDER, J EDWARDS, A JOHNSON
Aneurin Bevan University Health Board, Wales, UK

Objective: Paediatric patients with epilepsy reaching transition stage to adult neurology were only being offered one joint "handover clinic". Patients and their families had no preparation for this transition. Likewise, there was little preparation by clinicians for which issues needed discussion. A need to improve the transition care of patients was identified and the 'Ready Steady Go' transition model was chosen. Our team were a part of the EQIP pioneers to participate within the first paediatric epilepsy quality improvement collaborative pilot (RCPCH EQIP) in England and Wales, managed by the Epilepsy12. The purpose of the pilot was to provide 12 paediatric epilepsy teams with practical training and support and help them uncover the gaps in service provision and develop interventions that meet their specific needs. Our aim was 90% of 14 to 16 year olds with epilepsy to have been sent 'Ready, Steady, Go' questionnaires by May 2020.
Methods: In cycle 1, we established how patients and families would like to receive information about their healthcare. In cycle 2, we tested efficacy of the process by completing questionnaires with one patient in clinic, and with another patient by telephone. In cycles 3 and 4, we established a shared network folder for storing questionnaires and created a 'Watch list' of all transition patients to track process. In cycle 5, due to COVID-19 we had an additional task of piloting a video-clinic with 2 consultants, 1 specialist nurse, patient, and carers all in separate locations. Feedback was collected from all patients.
Results: 98% of all 14 to 16-year olds with epilepsy were sent the 'Ready, Steady, Go' questionnaires by May 2020. We have established a bi-monthly consultant led transition clinic and additional nurse led clinics to support this.
Conclusion: We have now embedded the routine collection of transition information into regular clinical practice.

Poster No. 194
Efficacy and safety of Perampanel in paediatric patients (aged 4–<12 years) with partial-onset seizures (POS) or primary generalised tonic-clonic seizures (PGTCS) who converted to monotherapy: A case series from study 311

A FOGARASI[1], LY NGO[2], A PATTEN[3], M MALHOTRA[4]
[1]Epilepsy Center, Bethesda Children's Hospital, Budapest, Hungary; [2]Eisai Inc., Woodcliff Lake, NJ, USA; [3]Eisai Ltd., Hatfield, Hertfordshire, UK; [4]Eisai Inc., Woodcliff Lake, NJ, USA

Objective: Perampanel is a once-daily oral anti-seizure medication (ASM) for POS and PGTCS. Study 311 (NCT02849626) was a multicentre, open-label study of adjunctive perampanel oral suspension in paediatric patients with POS (with/without secondarily generalised seizures [SGS]) or PGTCS. We report efficacy and safety data from patients who converted to perampanel monotherapy during Study 311 (Core and Extension A Phases).
Methods: Baseline demographic information were recorded and efficacy assessments included median percent change in seizure frequency/28 days from baseline and seizure-freedom rates. Safety assessments included reporting treatment-emergent adverse events (TEAEs).
Results: Overall, 4/180 patients converted to perampanel monotherapy. Baseline demographics were (gender/seizure type/concomitant ASM[s]): Patient 1 (aged 7): F/PGTCS/phenytoin; Patient 2 (aged 4): F/POS/rufinamide, lacosamide; Patient 3 (aged 10): M/POS/oxcarbazepine; Patient 4 (aged 9): M/POS/oxcarbazepine. Median total perampanel treatment duration in these 4 patients was 363 days (range, 337 to 367 days), of which patients were receiving perampanel adjunctive therapy for a median duration of 203.5 days (range, 186 to 244 days) before converting to perampanel monotherapy (median duration, 152 days; range, 118 to 171 days). Perampanel doses received by these 4 patients during adjunctive and monotherapy perampanel periods were: Patient 1, 6 and 4mg/day, respectively; Patient 2, 8mg/day for both; Patient 3, 14mg/day for both; Patient 4, 6 and 4mg/day, respectively. At Weeks 40 to 52, median percent reduction in seizure frequency/28 days from baseline was 100.0% for Patients 1–3 and 75.0% for Patient 4. Patient 2 achieved seizure freedom at Weeks 40 to 52. During adjunctive/monotherapy, 30 TEAEs occurred in these 4 patients; 23 occurred prior to monotherapy conversion and 7 occurred during monotherapy.
Conclusions: In this case series analysis, conversion to perampanel monotherapy provided efficacy and was generally well tolerated. Further investigation is warranted due to the small sample size.

Poster No. 195
Case report: Effective use of lacosamide in SCN2A epilepsy in an emergency setting

D NAGA, T SMITH, S NICOL, D RAM
Department of Paediatric Neurology, Royal Manchester Children's Hospital, Manchester, UK

Introduction: Traditional sodium channel blockers are generally effective in managing seizures in children with SCN2A-related epileptic encephalopathies. We describe a case of dramatic response to lacosamide despite poor response to multiple other therapeutic options in a critical care setting.

Case: Our case involves a female infant, who initially presented with refractory epilepsy in the neonatal period associated with burst suppression on her EEG. Subsequent investigations revealed a gain in function mutation in SCN2A. She initially had a reasonable response to carbamazepine and sodium valproate, but continued to have multiple daily episodes of short-lived seizures. At 8 months of age, she presented with a significant deterioration of seizure control. Her EEG showed evidence of tonic status epilepticus and she was loaded with intravenous phenytoin. Despite optimising the phenytoin with further boluses, she continued to have multiple seizures requiring intubation and ventilation. She continued to have frequent seizures until she was loaded with intravenous lacosamide 2mg/kg and commenced on rapidly escalating maintenance doses. She remained completely seizure free thereafter for over 12 weeks and has since had some breakthrough seizures, but much less frequent than before.
Discussion: Traditional sodium channel blockers such as carbamazepine, lamotrigine, phenytoin and sodium valproate are used as first-line agents in managing seizures in gain of function mutations of SCN2A. Lacosamide selectively enhances slow inactivation of sodium channels and may therefore be a useful add-on to other agents which predominantly affect fast-inactivated states. Intravenous administration allows rapid delivery in the critical care setting in patients with refractory status epilepticus. It has been described in literature to be helpful even in some neonatal cases of SCN2A-related epileptic encephalopathy.
Conclusion: Lacosamide is a safe and effective drug in managing refractory seizures in infants with SCN2A-related epilepsy when traditional sodium channel blockers have not been as effective.

Poster No. 196
Integrated seizure care pathway - A RCPCH EQIP Project

TYAGI[1], S TEKKI-RAO[1], V GANDHI[1], A JOSHI[1], H GOODGE[1], L STEVENS[2]
[1]*Paediatrics, Luton and Dunstable University Hospital, Luton, UK;*
[2]*Cambridgeshire Community Services NHS Trust, Cambridge, UK*

Introduction: Our team were part of the EQIP pioneers to participate within the first paediatric epilepsy quality improvement collaborative pilot (RCPCH EQIP) in England and Wales, managed by the Epilepsy12. The purpose of the pilot was to provide 12 paediatric epilepsy teams with practical training and support, held them uncover the gaps in service provision and develop interventions that meet their specific needs.
Objective: At the initial EQIP meet, our team chose to develop and implement an integrated care pathway for children admitted to Paediatric ward with epileptic seizures or seizures like events in order to facilitate consistent high quality care for these children.
Methods: The project started with short surveys of parents/patients, doctors and nurses. Based on these, three important areas of improvement were identified, namely, history taking, investigations and safe discharge. The existing acute admissions clerking document was improvised to accommodate these changes. For improving seizure history, a box with prompts, covering important points in a good seizure history, was inserted next to history taking section. For guidance to doctors on appropriate investigations and management, a flow chart was prepared and inserted. To ensure a safe discharge, a safety discharge check list was prepared and inserted at the end of the clerking document. These 3 sections went through several rounds of testing in ward and improvised.
Results: After several PDSA (Plan, do, study, act) cycles, a final clerking document, titled as Integrated seizure care pathway, has been rolled out in the department. We are noticing a much better seizure history and safety advice on discharge as well as improved parent/patient experience.
Conclusions: Based on our experience in this RCPCH EQIP project, we recommend initiation of Quality improvement projects in other Epilepsy units to improve team efficiency and quality of patient experience.

Poster No. 197
Evolving the Physician Associate role in epilepsy

AB BOWNESS, SM MARIGUDDI, FS SHORT
Paediatrics, Ormskirk Hospital, Lancashire, UK

Objective: To describe the new role of Physician Associates (PA) within a DGH Epilepsy team and provide a framework for developing the role for the future.
Introduction: PA's are medically trained professionals, who work alongside doctors and the other members of the Multidisciplinary team to provide care within the National Health Service. They are currently employed in a wide range of settings across primary and secondary care. As part of the National Epilepsy quality improvement program the Epilepsy team had identified gaps in provision due to CCG funding and also areas in which we could improve the service.
Method: To bridge gaps in service provision and service improvement the team found an innovative solution of adding a PA to the established team to further improve the service. The PA would contribute to history taking, examinations, idea sharing, telephone consultation and family discussions. They would also visit patients and schools in the area to provide teaching and support. All patients within the current Ormskirk cohort were considered when providing feedback for the team.
Results: The team received excellent team feedback from our patients using our national quality improvement feedback tool. A larger team has enabled discussion and learning on how to review and manage current patients. This has created a new allied health professional led clinic which can run in the absence of the consultant and thus ensure lesser waiting times.
Conclusion: The addition of enthusiastic PA has the potential to impact positively on the quality of care provided whilst supporting the gaps in Epilepsy nurse provision. We have shown that this improves quality outcomes such as efficiency and patent experience. We would propose further investments and inclusion of a PA in epilepsy teams nationwide.

Poster No. 198

Stimulant and non-stimulant drug therapy for people with epilepsy (PWE) and attention deficit hyperactivity disorder (ADHD): a Cochrane review

K YONG[1], C EATON[2], V WALTER[3], GK MBIZVO[3], S RHODES[2], RFM CHIN[1,2,3]

[1]Department of Clinical Neurosciences, Royal Hospital for Sick Children, Edinburgh, UK; [2]Child Life and Health, MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK; [3]Muir Maxwell Epilepsy Centre, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

Objective: To examine the effect of stimulant or non-stimulant drugs on seizure frequency and severity (primary outcome); ADHD symptoms; adverse events and withdrawal rates; cognitive state, general behaviour, and Quality of Life in PWE and ADHD.

Methods: The protocol for this ongoing review has been published. We carried out a comprehensive search for randomised controlled trials (RCTs) on stimulant and non-stimulant drugs in PWE and ADHD. Studies were screened by two independent reviewers. Data were extracted by one of the authors (KY). Seizure outcome analysis was on an intention-to-treat basis. Risk of bias, heterogeneity and sensitivity analyses are being undertaken.

Results: 88 studies were identified by database searching; 68 excluded by screening of title and abstracts. Twenty underwent full text review; 16 studies were excluded leaving four studies for final inclusion. Two involved methylphenidate, and one each with OROS-methylphenidate and Omega-3. There were no eligible RCTs on any other stimulant or non-stimulant drugs. Methylphenidate did not significantly increase seizure frequency compared to usual treatment in one study (n=30). Methylphenidate significantly improved Revised Conners' Teacher Rating Scale but not parent scores compared to placebo (n=10). Adverse events from methylphenidate usage did not result in medication cessation (n=40). A significant number of participants discontinued OROS-methylphenidate compared to placebo due to adverse events; higher doses were associated with increased seizure risk ratios (n=33). There was a significantly higher number of participants treated with Omega-3 with >50% reduction of seizure frequency and decreased monthly seizure frequency compared to placebo (n=56). Results of further analyses will be presented.

Conclusions: No reliable conclusions can be drawn on the effect of stimulant and non-stimulant medication for PWE and ADHD; high quality evidence is limited. There is some evidence that methylphenidate does not worsen seizure control but improves teacher-rated ADHD symptoms in PWE. More research is needed.

Poster No. 199

Ketogenic dietary therapy (KDT) initiation in the home setting – Does this influence adherence?

H CHAMPION, M CHITRE, Z DOWD, P HARIJAN, A MAW, N MILLS, APJ PARKER

Department of Paediatric Neurology, Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, UK

Introduction: In 2009 an expert consensus guideline for the management of children on KDT was published; the majority of centres supported initiating KDT in a hospital setting. In 2018 these guidelines were revisited and 92% of centres supported initiating KDT in the outpatient setting in selective situations.

Method: We compared the data for KDT compliance for children starting the diet across three time periods, using cessation of KDT as a proxy for adherence: (1) 2009 to 2015: 147 families were advised to start the diet in the hospital setting. (2) April 2017 to February 2020: 102 families could choose to start in the hospital or home environment. (3) April 2020 to June 2020: 12 families in the first 3 months of the COVID-19 'lockdown' advised to start at home. All case notes of consecutive patients from three specified time periods were reviewed. Percentage differences were analysed using the "N-1" Chi-squared test.

Results: Cessation of KDT within 3 months of initiation was a) 44/147 (30%) vs 32/102 (31%) p=0.8663 and b) 44/147 (30%) vs 5/12 (42%) p=0.3886. The numbers of children unable to complete the 3 month trial period were 15/147 (10%) vs 13/102 (12.7%) p=05057. Within the second group a higher proportion of those opting to start in hospital ceased therapy early, 6/37 (16%) compared to 7/65 (10.7%), however this was not clinically significant (p=04406).

Conclusion: In the two large groups of children studied, starting KDT in the home setting was equally as effective as starting in hospital at achieving adherence at 3 months. In the smaller group starting therapy remotely during the COVID restrictions there was a trend towards less adherence; this may reflect their epilepsy, change to support, teaching using remote platforms (rather than in person), difficulties accessing novel foods or small sample size.

Poster No. 200

A comprehensive review of vagal nerve stimulation use and outcome in paediatric patients at a tertiary paediatric neurology centre

MH HIRA, HA AKBARI, MC CHITRE

Paediatric Neurology, Addenbrookes Hospital, Cambridge, UK

Objective: To review the referral pathway and outcomes of Vagal Nerve Stimulation (VNS) in Paediatric patients with epilepsy

Methods: This was a retrospective chart review including all patients under the age of 16 who were referred to the VNS service between January 2018 to June 2020 (30 months).

Results: A total of 62 patients were identified, out of which 16 completed pathway of referral, neurological, neurosurgical assessment, and VNS Insertion. Thirty new referrals were assessed for VNS in this time frame, out of which 27 underwent Neurosurgical assessment. Pathway waiting time from time of referral to Neurological assessment was 2 to 4 weeks on average and 4 to 8 weeks on average for neurosurgical assessment. VNS models used were Sentiva 1000 and 106 Aspire. Majority showed good response to VNS; 5 children showed 50% reduction in seizure frequency. Patients with genetic generalised epilepsy presenting with generalised tonic clonic seizures showed the best response. Post-operative complications included shortness of breath, voice change, cough and headache, and 2 patients had wound infections. As expected, there was no significant difference in seizure control and side effects between the two devices. However, the remote programming capability of the Sentiva 1000 offered significant benefit with reduced hospital and improved school attendance especially during the Covid 19 pandemic. Unfortunately, we had 2 cases of SUDEP involving patients with severe disability.

Poster No. 201

Antiepileptic drug weaning after ketogenic diet initiation in infancy and early childhood

M GOGOU[1], T NEMANI[1], C CHIANG[2], Z SIMPSON[1], I STEANE[1], N SCHOELER[2], JH CROSS[1,2], C ELTZE[1], S PUJAR[1]

[1]Great Ormond Street Hospital for Children, London, UK; [2]Clinical Neurosciences, Institute of Child Health, London, UK

Objective: The introduction of ketogenic diet (KD) in children with pharmacoresistant epilepsy could allow reduction in anti-seizure drug (ASD) load and any associated adverse events. We present a single centre's experience on weaning ASD after KD initiation in children with epilepsy aged under 6 years.
Methods: Medical records (e.g. clinic letters, progress notes, discharge summaries) were retrospectively reviewed of children 1 month to 6 years started on KD between January 2013 and June 2018 at Great Ormond Street Hospital. Logistic regression was conducted to investigate whether demographic, diagnosis-related or seizure-related factors predict successful ASD withdrawal (i.e. without change of seizure frequency requiring re-introduction of the ASD).
Results: Of 58 children 49 were included (40.8% female, median age of seizure onset 4 months, median age at KD initiation 20.7 months). Nine were excluded (3 with glucose transporter type 1 deficiency without seizures and 6 treated for <3 months including 1 with refractory status epilepticus). Withdrawal of ≥1 ASD(s) was attempted in 34/49 (69.3%), 21/34 KD responders (>50% seizure reduction) and 11/34 seizure-free or >90% seizure reduction at this time. Withdrawal of ≥1 ASD(s) was achieved in 24 children (70.5%). Median time on KD before withdrawal attempt of the 1st ASD was 3.25 months. Gender, age of seizure onset, and KD initiation, seizure type (motor vs non-motor), history of spasms, aetiology (genetic vs non-genetic), number of ASDs and KD duration were not significantly associated with successful withdrawal. Seizure reduction <50% at 3 months on KD was not related to subsequent successful ASD withdrawal. There was no significant difference in seizure outcomes at 12 and 24 months irrespective of ASD withdrawal.
Conclusions: Withdrawal of ≥1 ASD was successful in many children after KD initiation. Success of ASD withdrawal was not affected by demographic and clinical variables, including seizure outcome at 3 months after KD initiation.

Poster No. 202

Extending the phenotype of GRIN2A related seizure disorders

CP WHITE, S TUOHY

Department of Child Health, Swansea Bay University Health Board, Swansea, UK

Background: The GRIN2A gene encodes the glutamate-binding GluN2A subunit of the NMDA receptor in the excitatory synapsis. GRIN2A gene mutations have been reported in a variety of childhood epilepsies including epilepsy with centro-temporal spikes, atypical childhood epilepsy with centro-temporal spikes, epileptic encephalopathy with continuous spike-and-wave during sleep and in Landau Kleffner syndrome.
Case report: We present a child whose initial presentation with what was considered to be elective mutism and who later developed repeated episodes of nonconvulsive status. Currently he has occasional clusters of focal seizures associated with behavioural deterioration and a severe intellectual disability. The patient was adopted from a birth mother with Von Hippel Lindau syndrome and epilepsy (about which little is known). He was reported to have mild speech delay before becoming mute following minor surgery at the age of 3 years 5 months. Investigation of this revealed a grossly abnormal awake EEG with frequent focal and generalised discharges. He was treated with steroids which led to slow improvement in his language skills. The patient's overt seizures started 2 months after this loss of language. He had a generalised tonic clonic seizure that appeared to have been provoked by flashing lights. He continued to have vacant episodes and occasional GTCs until he presented 7 months later in nonconvulsive status. This was associated with language regression. He continued to have episodes of language regression initially associated with nonconvulsive status and later with continuous spikes and waves during slow sleep (CSWS) only. He was found to have a nonsense mutation in the GRIN2A gene on epilepsy gene panel testing, having previously had a normal array CGH.
Conclusion: The association between disorders on the epilepsy-aphasia spectrum and mutations in the GRIN2A gene is well recognised as is the relationship with CSCW but diurnal nonconvulsive status has not been reported previously.

Poster No. 203

Efficacy of ketogenic diet in new onset super-refractory status epilepticus due to a de novo DNM1L mutation

MR SMITH[1], S CHOWDHURY[1], C EDGECUMBE[1], J WADSWORTH[1], J GADIAN[2], S JAYAWANT[1], N MCCREA[1], A MOLLETT[1], S RAMDAS[1], R RATTIHALLI[1], R TAILOR[3], M TORRES[1], M HOFER[1], A MOLYNEUX[1], R JOSEPH[1], A ROMSAUEROVA[1], D O'SHEA[1], L LOONG[1], J BAPTISTA[4], E BLAIR[1], V NESBITT[1]

[1]Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]King's College Hospital NHS Foundation Trust, London, UK; [3]Upton Hospital, Slough, UK; [4]Royal Devon and Exeter NHS Foundation Trust, Exeter, UK

Clinical presentation: A 5 year old male with prior normal development, presented with afebrile new onset super-refractory status epilepticus (SE). First signs were of generalised rhythmic myoclonus with preserved consciousness and awareness. Over the following 2 weeks SE persisted despite combination therapy with anaesthetic agents (Midazolam, Ketamine, Thiopentone), immuno-suppression (iv Methyl Prednisolone, plasmapheresis), and conventional AEDs (Levetiracetam, Phenobarbitone). The introduction of the ketogenic diet (KD) was associated with slow steady improvement. He was able to be discharged after 10 weeks, by which time he was seizure free for 3 weeks, on combination therapy with Levetiracetam, Phenobarbitone, Zonisamide and ketogenic diet. He had regained the ability to stand unaided and speak. Cognition appeared relatively preserved.
Investigations: Initial MRI of the brain and spine normal. CSF analysis (including lactate) normal. Repeat imaging revealed transient abnormalities in the thalami, lentiform nuclei and hippocampi. EEG revealed diffuse high-amplitude polyspike and wave potentials discharging quasi-periodically at c1Hz, time-locked to myoclonic jerks involving variably the distal or proximal limb muscles of either side. Muscle biopsy revealed significant number of cytox (COX) negative fibres, increased lipid content in

type I fibres, and type I fibre predominance, suggestive of mitochondrial disease. Trio exome sequencing identified a de novo heterozygous pathogenic missense variant in DNM1L.
Discussion: DNM1L is a GTPase that is involved in mitochondrial fission. It is associated with neonatal hypotonia, delayed psychomotor development, early-childhood onset of encephalopathy and refractory epilepsy, but has also been described in older children with prior normal or near-normal development. New onset super-refractory SE (of all causes) is associated with a 25% mortality. Our experience suggests a good outcome is possible, and supports the early use of the ketogenic diet.

Poster No. 204
Bilateral Rasmussen: two new case reports and review of literature

L D'ARGENZIO[1], J GENCARELLI[1,4], M CONNOLLY[3], L MING[1], M KALIAKATSOS[2]
[1]Department of Paediatric Neurology, Evelina Children's Hospital, London, UK; [2]Department of Paediatric Neurology, Great Ormond Street Hospital, London UK; [3]Division of Neurology, Department of Pediatrics, BC Children's Hospital, Vancouver, British Columbia, Canada; [4]Paediatric Unit, Medical Department, University Hospital Arcispedale Sant'Anna, Ferrara, Italy

Background: Rasmussen Encephalitis (RE) is a rare form of immune-mediated encephalitis characterised by progressive, typically uni-hemispheric inflammation and atrophy with gradual onset of neurological dysfunctions. RE can involve both hemispheres after initially affecting one hemisphere or may have bilateral involvement from the onset.
Objective: Here we report two new paediatric cases of bilateral RE with signs of neuroradiological and clinical involvement of both hemispheres. We also reviewed the literature and summarised all previous reports of bilateral RE.
Results: Our first case presented at 2.5 years of age with 2-month history of progressive left spastic hemiplegia. Her brain MRI showed typical changes of RE in the right hemisphere but also subtle changes in the left insular and temporal areas, which progressed in subsequent scans. Seizures began 2 months after the initial presentation and continue to progress despite antiepileptics and neuroimmunomodulatory treatment. Our second case presented aged 7, with subtle motor difficulties in the left leg over a 5-year period and a recent onset of sub-continuous movement of the right arm. Patient did not respond to medical treatment and he continue to show motor and cognitive decline over time. Finally, we reviewed 21 cases of bilateral RE reported in the literature. All cases but two showed a unilateral onset and then developed contralateral signs associated with bilateral cortical lesions. Age of onset (average 6 years old) did not differ from classical RE but outcome appear to be poor, even in those cases treated with surgical intervention.
Conclusion: Bilateral RE is a rare but challenging disorder which does not appear to respond to medical treatment and for which surgical intervention might be helpful but may not have the same effectiveness demonstrated in unilateral cases.

Poster No. 205
Evaluation of a paediatric ketogenic diet service in Ireland

DC CLIFFORD, JC CROWLEY, NM MCSWEENEY, O O'MAHONY
Paediatric Department, Cork University Hospital, Cork, Ireland

Objective: A retrospective study to assess our paediatric ketogenic diet service in a quantitative and qualitative manner. This will improve our adherence to guidelines for biochemical monitoring of these patients and will assist in improving patient experience.
Methods: A list of paediatric patients who have trialled the ketogenic diet since the service was established at Cork University Hospital in 2016 was obtained. To assess biochemical monitoring, each patient was searched using iSoft iLab Laboratory Information Management System and results were compared to the recommended monitoring schedule. Surveys relating to patients' experience of the service were distributed and recurring themes will be assessed and highlighted.
Results: The majority of our 17 patients had the required baseline bloods documented prior to commencing the diet. 82% had a baseline FBC, U&E, LFT, calcium, phosphate and acylcarnitine. 76% had a baseline coagulation profile, 71% had lipids and 65% had baseline glucose. Baseline carnitine was recorded for 53% and 76% had Vitamins A and E assessed. 65% had a baseline vitamin D. As treatment progressed biochemical monitoring became less consistent with U&E and LFTs checked in 69%, 46% and 44% at 3 months, 6 months and six-monthly, respectively. Recommended, annual non-essential bloods such as vitamin C, copper and selenium were checked in just 11%. Overall, patients had a mean of 51.9±18.1% of the indicated bloods. Qualitative results pending.
Conclusion: While baseline bloods are documented for most of our patients, this is not sustained throughout treatment. There may be several reasons for this including the volume and frequency of biochemical monitoring or the labour-intensive process of following-up results. Having an assigned staff member designated to monitoring bloods throughout treatment would improve adherence to guidelines for scheduled biochemical monitoring and would allow safe expansion of our ketogenic diet service.

Poster No. 206

NORSE: a case series of 4 patients presenting to Leeds Children's Hospital

A HENDERSON[1], AM CHILDS[1], S HUSSAIN[1], H MCCULLAGH[1], M RAY[1], D WARREN[2], H CLIFFE[2], K PYSDEN[1]

[1]*Department of Paediatric Neurology, Leeds Teaching Hospitals Trust, Leeds, UK;* [2]*Department of Radiology, Leeds Teaching Hospitals Trust, Leeds, UK*

Introduction: Status epilepticus (SE) results from failure of mechanisms responsible for seizure termination or from initiation of mechanisms, which lead to abnormally prolonged seizures. It can be associated with long-term consequences, including neuronal death, neuronal injury, and alteration of neuronal networks. It is estimated to occur in 10 to 40 per 100,000. 30% of SE persist even after treatment with two medications: this is known as refractory status epilepticus (RSE). RSE can occur in epilepsy; but also in those without epilepsy due to a stroke, brain injury, infection, or tumour. New onset refractory status epilepticus (NORSE) occurs when the cause for RSE remains unidentifiable beyond 72 hours. The most common aetiology is autoimmune, however up to half remain cryptogenic.
Objective: We describe the course, EEG findings, neuroradiology, management, and outcomes in four cases of NORSE, presenting at Leeds Children's Hospital between 2014 and 2020.
Cases: The cases were aged 10 to 16 years and were previously fit and well. Initial presentation was with either generalised status epilepticus or acute confusional state, with a history of preceding fever in some cases. Three required intubation and ventilation, with length of stay ranging from 7 to 219 days. The number of anti-epileptic drugs ranged from four to eight. All patients had abnormal EEG, some showing evidence of migrating focal seizures and others with a more diffuse and severe cortical pathology. MRI showed features consistent with NORSE. All patents received methylprednisolone and Immunoglobulins. Other treatments included ketogenic diet, anakinra and toculizumab. One patient died on day seven. The others continue on anti-epileptic medication and have ongoing seizures and changes in their pre-morbid behaviour.
Conclusions: Management of NORSE is challenging, mortality and morbidity is high. A larger review of patients may help to identify patients earlier and common effective treatment strategies, to help shape future management of these patients.

Poster No. 207

Vitamin D prevention in children with epilepsy with and without neurodisability; Clinical audit on local practice at a district general hospital. It is time for national guidance from BPNA

M ELGAMAL, TS RAO

Bedfordshire Hospitals NHS Trust, Luton, UK

Objective: Several factors contribute to Vitamin D deficiency in epilepsy patients especially antiepileptic drugs which interfere with vitamin D metabolism. Published literature showed that 72% of children with epilepsy had low Vitamin D levels compared to 50% of healthy controls. We have evaluated our current practice of monitoring bone health and vitamin D supplementation in children with epilepsy at a district general hospital auditing against regional network guidelines.
Methods: Data have been collected retrospectively from electronic records including blood results and previous imaging. Patients have been divided into two groups; Epilepsy without neurodisability (n=29) (Group A), and epilepsy with neurodisability (n=28) (group B). The results were mapped against national and regional guidance.
Results: Observational analyses revealed that only 45% of patients in group A have been on vitamin D prevention, compared to 85% in the other group. However, 8% of Group B have been on nutritional formulas with suboptimal dose of vitamin D. Patients who had their vitamin D level checked in group A were 34%, with 10% of them had insufficient vitamin D levels whereas 46% had their levels checked of whom 23% of them had insufficient levels in group B. None of the patients in group A had symptoms of vitamin D deficiency compared to 18% in group B. And, 80% of the symptomatic patients had vitamin D treatment with long term maintenance dose.
Conclusions and recommendations: We identified that less than 50% of children with pure epilepsy were receiving vitamin D supplements but better attention was paid for those with neurodisability. We suggest that all epilepsy units should audit their own practice. Although there were some regional network guidelines exist across the UK, national guidance for children with epilepsy is lacking and it is time for standards.

Poster No. 208

Dual pathology in epilepsy patients - a challenging new norm?

SK KHAMIS, AM MALLICK, SH HOSAINEY, MG GAINSBOROUGH, AM MAJUMDAR

Bristol Royal Hospital for Children, Bristol, UK

Introduction: The diagnosis of epilepsy, once seemingly straightforward has now become a challenge. It is clear that no universal test exists to aid in reaching a conclusive diagnosis.
Case report: We report a child who presented with tremors at the age of 9 months, subsequent difficult to treat epilepsy, ataxia, developmental delay and loss of skills. She was initially treated for encephalitis due to a suspected infection and further investigation into her diagnosis including epilepsy and severe delay NGS panel revealed no clear pathogenic variant. She was however found to have two separate deletions on long arm of Chromosome 1 (1q21.1) and Chromosome 17 (17q.25.3), not known to be of clinical significance. An MRI brain showed bilateral hipoccampal sclerosis (right > left) in keeping with the changes seen on her EEG. In view of her neurological decline and uncontrolled epilepsy she underwent assessment for epilepsy surgery and subsequently right anterior medial temporal lobectomy. During her postoperative period she developed seizures and left hemiparesis. MRI brain done at that time revealed right side cerebral edema and this led to a clue that channelopathy might be the causative factor. Subsequently we sent for further tests and CACNA1A mutation was detected.
Conclusion: One of the complexities in reaching a diagnosis in neurological patients is the changing clinical picture and continuous evolution of symptoms. However with the advancement of genetic testing methods comes new challenges. It is vital to continuously review our diagnosis despite reaching a final one. Dual pathology is a conundrum which we will be facing even more with the advancement and availability of diagnostic tests.

Poster No. 209

An unusual case of worsening epilepsy in a child with SCN8A mutation on a sodium channel blocker

K LOTHA, M TAYLOR, S HUSSAIN
Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK

Objective: SCN8A encodes for voltage-gated sodium channel α subunits; most mutations have an activating effect. There is evidence in the literature of response to sodium channel blockers such as carbamazepine, oxcarbazepine and phenytoin; with deterioration reported to occur on levetiracetam. Our case is one where a child with early onset SCN8A-related epileptic encephalopathy demonstrated disimprovement on lamotrigine and subsequent improvement when discontinued.
Methods: A retrospective review of the patient's paper and electronic medical records.
Results: A 3-year-old male, born at 36 weeks gestation after induction for foetal bradycardia and an uneventful neonatal course, presented with early onset febrile seizures followed by hemi-clonic afebrile seizures. He subsequently developed multiple seizure phenotypes: focal with impaired awareness, generalised tonic-clonic, atonic and absence seizures. Family history identified an aunt with cerebral palsy but there was no significant epileptic pedigree. The patient had a background of global developmental delay and the emergence of epilepsy was associated with regression and loss of previously acquired language skills and unaided walking. Clinical examination elicited truncal ataxia with jerky head and tremulous limb movements. Sodium valproate was commenced and his development improved but due to a persisting seizure burden lamotrigine was introduced. One month post commencing lamotrigine he developed disimprovement of seizure control associated with prolonged periods of reduced responsiveness and re-emergence of developmental regression. After commencing lamotrigine an early infantile epileptic encephalopathy gene panel yielded a likely pathogenic SCN8A missense variant, NM_014191.3: c.2890G>T p.(Gly964Cys). Lamotrigine was weaned and clobazam was introduced; associated with clinical improvement in both seizures and developmental progression.
Conclusion: This case presents a severe clinical phenotype of SCN8A encephalopathy with clinical deterioration with lamotrigine that has not previously been reported in the literature. This case demonstrates that sodium-channel blockers will not always improve seizures and conversely can cause deterioration in seizures in patients with SCN8A.

Poster No. 210

Audit - Adherence to NHS England CESS (Children Epilepsy Surgery Service) referral guidelines

B AZADI, V TYAGI, S TEKKI-RAO
Epilepsy, Luton & Dunstable Hospital, Luton, UK

Objective: To evaluate the adherence to the CESS referral guidelines in a cohort of children newly diagnosed with epilepsy at Luton & Dunstable hospital in the years 2015 and 2016.
Methods: We were provided with the data of all the children who had EEG in the year 2015 and 2016 by our Neurophysiology department. This data was reviewed to choose children newly diagnosed with epilepsy over these 2 years. Their case records were then reviewed against CESS referral standards to identify patients that met the criteria.
Results: 97 children were identified with the new diagnosis of epilepsy made in 2015 and 2016. Out of these, 9 (5 girls and 4 boys) met the criteria for CESS referral. 6 were referred to CESS at GOSH and 3 were not referred. Out of the six that were referred, all of them were reviewed within 6 months at GOSH and one of them had epilepsy surgery. For the other 5, surgery was not advisable due to various reasons like aetiology, epilepsy type and good control of seizures with medical therapy. For the 3 patients that met the criteria (Focal seizure with unilateral lesion on MRI), CESS referral was considered but they were not referred as seizures were well controlled with medications.
Conclusions: Our results showed that we referred around 70% of the patients that met the criteria. We aim to improve our referral to 100% in next 2 years. All Epilepsy units need to audit their practice to ensure timely referral of these children to CESS is made.

Poster No. 211

UK North West profile of Epidyolex use for refractory seizures in children

E HASSAN, I DESAI, R SOPONSKI, D MUTHUGOVINDAN, HJ TAN
Paediatric Neurology Department, Royal Manchester Children's Hospital, Manchester, UK

Introduction: Medicinal cannabis has been gaining interest in clinical fields. Following the results of phase III trials, NICE recommended the use of Epidyolex for severe drug resistant epilepsy at the end of 2019.
Methods: Retrospective review of all our patients prescribed CBD in the form of Epidyolex. Details collated included epilepsy diagnosis, concomitant anti-seizure drugs (ASDs), percentage seizure frequency (SF) change, adverse effects and reasons for discontinuation of treatment.
Results: Sixteen patients were included; 56.25% (n=9) had a syndromic diagnosis of Lennox Gastaut (LGS), 31.25% (n=5) Dravet (DS) and 12.5% (n=2) other diagnoses. The mean/range time on CBD treatment was 9.4 (3–20) months. The mean/range dose of CBD used was 11.1 (5.4–20) mg/kg/day. Overall, 37.5% (n=6) had >30% to <75% reduction in SF, whilst 31% (n=5) had a >75% reduction. In children with DS (n=5), >75% SF reduction including drop seizures was seen in one patient (20%), >30% to <75% reduction in two (40%) and no improvement in two (40%). In children with LGS (n=9), >75% reduction in SF including convulsive seizures was seen in three patients (33.33%), >30% to <75% reduction seen in four (44.4%) and no improvement in two (22.2%). Among the other subgroups, patient with FIRES showed >90% improvement but patient with CMD had no clear improvement. The main adverse effects were vomiting (n=3) and behavioural difficulties (n=5); none of which led to CBD discontinuation. Three patients stopped CBD due to worsening seizures (n=1) and ineffectiveness (n=2).
Discussion: NICE recommends discontinuing CBD if seizure reduction is ≤30% after 6 months of treatment. 68.75% (n=11) of our patients had a reduction in SF >30% and the patients whose SF had not improved immediately continue to have close monitoring. The important task of monitoring the effectiveness and safety of this newly licensed drug was made possible by the support of our epilepsy-specialist nurse.

Poster No. 212

Developing and standardising quality of life tools for children with epilepsy and severe disabilities

FJ WILKINSON[2], APJ PARKER[1,2]
[1]Addenbrooke's Hospital, Cambridge, UK; [2]Clinical Medical School, University of Cambridge, UK

Objectives: There is no standardised assessment of quality of life (QOL) for children with epilepsy and severe disabilities. The Cambridge-London Quality of Life Questionnaire (CLQ) for children with severe epilepsy has been piloted, but not standardised. We aimed to identify what is needed to produce a useful quality of life assessment for this population.
Methods: A systematic literature search was performed to: (1) Identify which key criteria must be achieved to validate a QOL tool. (2) Assess existing questionnaires on QOL in children with epilepsy and to analyse them for their utility in a population of children with severe disabilities. (3) Improve and validate the CLQ.
Results: Three existing QOL tools were identified. None were shown to be appropriate for the population of children with epilepsy and severe disabilities. An evidence based, methodical and effective pathway has been proposed to develop and validate QOL tools such as the CLQ.
Conclusion: With a larger trial of the modified CLQ, the systematic proposal recommended may make the CLQ a statistically significant and clinically useful tool for a population of children with epilepsy and severe disabilities.

Poster No. 213

Clinical profile, MRI and EEG findings in children with epilepsy at a quaternary hospital in Durban, South Africa

AW KAMUNYA[1,2], L MUBAIWA[1,2]
[1]Inkosi Albert Luthuli Central Hospital, Durban, South Africa; [2]Department of Pediatric Neurology, University of KwaZulu Natal, Durban, South Africa

Background: Electroencephalography (EEG) and neuroimaging are important investigations in the diagnosis of epilepsy. The EEG is a sensitive method to detect epileptogenicity of a brain lesion. MRI is used to identify a potential underlying brain epileptogenic structural lesion. There is a paucity of information on the diagnostic utility of EEG and MRI in the developing countries and South Africa.
Objectives: To evaluate the correlation between the clinical profile, EEG, and MRI brain abnormalities in children with epilepsy. To compare the diagnostic yield of MRI and EEG data.
Methods: A retrospective analysis of electronic medical records 123 children aged 1 month and 12 years attending epilepsy service between March 2019 to March 2020. Investigations were an EEG after two unprovoked seizures and an elective MRI of the brain within the first 6 months of seizure onset. Chi-square test of significance ($p<0.05$) was used to test for the difference in proportion. The correlation between MRI brain and EEG was studied using Mcnemar's test.
Results: 123 patients identified with abnormal EEG in 92 (74.8%) and 78 (63.4%) had potential structural epileptogenic lesions on MRI brain. This were focal epileptiform discharges (27.6%) and cortical atrophy (17.1%). Generalized onset epilepsy was observed in a majority of the patients, 37.4% (n=46). The significant clinical predictors of an abnormal EEG were focal onset epilepsy ($p<000.1$) and the presence of neurological deficits ($p=0.035$). The significant clinical predictors of MRI lesions were microcephaly ($p=0.034$), focal onset epilepsy ($p=0.001$), and therapy (monotherapy, $p=0.032$, and polytherapy, $p=0.048$.) Specific EEG abnormalities were not associated with MRI lesions ($p=0.08$).
Conclusions: Focal onset epilepsy is significant clinical predictor of abnormal EEG and MRI brain. An MRI brain is an important investigation in epilepsy and is more sensitive than an EEG. Developing countries should prioritise neuroimaging in treatment of epilepsy.

Poster No. 214

Photosensitivity in focal epilepsy

P AHMED, S BOYD, S SUDHAKAR, K DAS
Great Ormond Street Hospital, London, UK

Objective: To highlight the occurrence of photosensitivity in children with focal epilepsies and to correlate with imaging findings.
Methods: This was a retrospective case review of all patients with focal epilepsy and associated photosensitivity, evaluated at Great Ormond Street Hospital, London from January 2004-June 2020.
Results: 26 children with focal epilepsy and photosensitivity were identified. Photosensitivity was graded as 1 in 5 cases, grade 2 in 7 cases, grade 3 in 1 and grade 4 in 9 cases. In 4/26 cases there was no reference to the grade in the EEG report. The photoparoxysmal response was reproducible in 14/26 (54%) cases and outlasted the stimulus in 12/26 (46%) cases. 8 children (31%) experienced a clinical seizure during photic stimulation. An isolated habitual seizure was captured in one patient during the recording. 16/26 (62%) of children had abnormalities on imaging. A focal lesion was seen in 13 of these: posterior predominance in 6/13 (46%) cases, temporal lobe in 2/13, left hemisphere in 2/13, frontal in 1/13, fronto-parietal in 1/13, frontal, parietal and temporal lobe lesions in 1/13. In 6/9 (67%) cases there was a correlation between the ictal EEGs and the MRI findings.
Conclusions: The occipital cortex is implicated as the primary epileptogenic area in children with photosensitive epilepsy. Our findings reflect this to some extent with a posterior lesion seen in 46% of cases. However, this is not exclusive, and lesions in other brain areas (54%) can also be associated with photosensitivity. Although traditionally photosensitivity is believed to be a feature of generalised epilepsies, it needs to be looked for in a wider range of epilepsies, in keeping with current concepts of disseminated abnormal neuronal networks underlying epileptic disorders. These findings also highlight the need for providing appropriate preventive and protective advice regarding photosensitivity to those children who are symptomatic.

Poster No. 215

Water immersion-related seizures: a case report and literature review

SH HAZAL, JF CANLAS, D CHANDRAN, MAS AHMED
Paediatric Department, Queens University Hospital, Essex, UK

Background: Water immersion-related seizures (WIRS) are rare reflex epilepsy. Over the last 10 years, our data helped us to

identify only one patient with WIRS. The authors will present literature findings on this unique condition.
Case report: An 11 month old healthy boy presented with a few months history of nine seizures that occurred exclusively during bathing. All seizures occurred within few minutes of having a bath. First he goes quiet, not responding, not falling, repetitive lip smacking and lips may turn blue. Birth and family history, neurodevelopment and neurological examination are unremarkable. Assessment confirmed that the seizures are not related to water temperature. During admission, he had similar bath – related seizure during which oxygen saturations dropped to subnormal level, whilst heart rate remained within normal limit. Interictal EEG, ECG and basic blood tests were normal. Brain MRI showed a non-specific focus of abnormal signal within the left centrum semi-ovale. Four months follow-up showed: (1) Seizure freedom on avoidance of having a bath or shower; (2) washing face, rinsing head or short shower (1–2 minutes) led to no seizure; (3) longer shower caused similar seizures; and (4) seizures occurred irrespective for water temperature.
Comment: Our assessment provided strong evidence of water (bath or shower) induced epileptic seizures. Other aetiologies for bath-related paroxysmal disorders were excluded. Although it is a rare disorder but reported in about 3.5% of all epilepsy cases in India, which links it to genetic and cultural predisposition. Its mechanism remains unknown. Reflex anoxic seizures, long QT syndrome, and cyanotic breath-holding spells could precipitate WIRS; however, there are limited or no reports on the assertion. There is a knowledge gap about the triggers of WIRS, and more studies are needed to build on the current information.

Poster No. 216

Are you tuned in? The challenges of seizure identification in children with learning disability – a potential for video-based care-pathway

M HUTCHISON[1], G BUXTON[2], C BRAND[3], A MCLELLAN[4], J SHETTY[1,4]
[1]*University of Edinburgh, Edinburgh, UK;* [2]*Royal Hospital for Sick Children, Edinburgh, UK;* [3]*Paediatric Epilepsy Nurse Consultant, Royal Hospital for Sick Children, Edinburgh, UK;* [4]*Paediatric Neurologist, Royal Hospital for Sick Children, Edinburgh, UK*

Objective: Epilepsy is common in children with learning disability (LD) and recognising seizures can be challenging. We aim to explore the challenges parents/carers face in seizure identification within children with co-existing epilepsy and LD.
Methods: Eligible participants attending a tertiary epilepsy clinic were enrolled to the study with written consent. Qualitative interviews were carried out by a single interviewer. Transcribed verbatim, these transcripts were analysed. Themes and subthemes were drawn to reflect the findings. Each transcript was read and discussed by two members of the research team. NVivo 12 was the software used to assist data analysis
Results: A total of 10 hours data gathered from 8 participants. The importance of knowing the child's normal and recognising changes to this baseline was consistently mentioned. All participants reported that being 'in tune' with their child assisted in seizure recognition. Most felt that health care professionals were poor at recognising seizures within their children. Participants had mixed thoughts on the difficulty the presence of a learning disability provides to seizure recognition. The severity of the learning disability and the seizure type were the two main variables discussed.
Conclusions: Knowing the child well and understanding the normal behaviour of the child as an individual is crucial to seizure recognition. A detailed description of 'normal' behaviour and seizure presentation stored within the child's medical notes may assist health care professionals in improving seizure recognition. Our study highlights the potential benefit of a video-based care pathway, where videos could be used to illustrate examples of normal behaviour and seizure activity. Children with LD are likely to be looked after in multiple settings by different staff in school, respite and residential care settings. A video care plan is likely to reduce the chance of misdiagnosis normal behavior as seizures or failure to correctly identify epileptic seizures.

Poster No. 217

Behavioural problems in childhood epilepsy measured using The Child Behavior Checklist (CBCL) - A systematic review

YA RASHID[1,3], FJ KIRKHAM[1,2]
[1]*University of Southampton, Southampton, UK;* [2]*UCL Great Ormond Street Institute of Child Health, London, UK;* [3]*University of Edinburgh, Edinburgh, UK*

Background: Epilepsy is diagnosed when an individual experiences 2 or more unprovoked seizures. Approximately 1 in 4 epileptic children experience behavioural problems. Many different questionnaires can be used clinically to measure behaviour in children such as the Strengths and Difficulties questionnaire and the Conner's Parent Rating Scale. However, we decided to focus on behaviour measured using the Child Behavior Checklist. Examples of behaviours measured in the CBCL include anxiety/depression, withdrawal/depression and aggressive behaviour. Additionally, specific versions of the CBCL also contain unique subscales, for example the 2 to 5 years version provides data on sleep problems and emotional reactivity.
Aims: The primary aim of this study is to determine whether children with a range of epilepsies exhibit more behavioural problems than controls and to see how behaviour changes over time.
Methods: Articles relevant to our aims were obtained by searching through the scientific databases MEDLINE, EMBASE, Psychinfo and Scopus. All of the articles included had to have compared epileptic children to controls. Articles which looked at the effect of surgical intervention were excluded.
Results: We found 13 articles which fit our inclusion criteria. Most studies suggested that epileptic children exhibited more behavioural problems than controls. However, there were some instances where controls demonstrated more behavioural problems. Furthermore, it was shown that behaviour did improve over time in the cases and maternal anxiety was shown to be an influential factor on the degree of behavioural problems. Finally, we grouped studies with cases of the same type of epilepsy or epileptic syndrome and saw certain behavioural problems more commonly in the cases than the controls.
Conclusions: Even though epileptic cases did demonstrate more behavioural problems than the controls, maternal anxiety had an effect and behaviour in the cases did get better with time.

Poster No. 218

Transition of young people with epilepsy - are we doing it right?

SSK DHULIPALA, H SREENIVASA
Wrightington, Wigan and Leigh NHS Foundation Trust, Wigan, UK

Aims: (1) Young people with epilepsy have an agreed transition period during which their continuing epilepsy care is reviewed jointly by paediatric and adult services. (2) The need for continuity of care during transition from paediatric to adult services is particularly important for young people managing the physical and mental transition from adolescence to adulthood. (3) To study the current transition service in paediatric epilepsy against NICE quality standards. (4) To identify good practice, gaps and develop a more comprehensive transition pathway and to set targets to achieve the desired results

Methods: Electronic case notes and clinic letters of 43 patients were reviewed over a period of 4 years between 2015 to 2018.

Results: All children and young people seen in Paediatric epilepsy clinic have been appropriately transitioned to adult services except 2 (one completely discharged and not on treatment, the other one – care transferred to local epilepsy service/GP). Age range when seen in transition clinics was 16 years 5 months to 18 years 10 months. Compliant with NICE guidance quality standards of transition of Paediatric epilepsy patients. We are the only Paediatric Unit in the region with appropriate Transition Service for children with epilepsy apart from an adult regional neurosciences centre and a tertiary children's centre.

Recommendations: Earlier Transition to be planned if possible so that they are transitioned before 18 and possibly to do more transition clinics. Patients seen at peripheral epilepsy clinic to be encouraged to attend teenage epilepsy clinics. To move patients from General Epilepsy clinic to Teenage Epilepsy clinics where appropriate. Improve documentation about who was present in the clinic which will help when re-auditing.

Poster No. 219

Clinical profile and underlying causes of focal epileptic seizures in Sudanese children

SMMA MAGZOUB[5], MEMA MAGZOUB[1], MSMA MAGZOUB[2], MAE ELSEED[3,4,5], IN MOHAMMED[4,5]
[1]College of Medicine and Health Sciences, United Arab Emirates University, Alain, UAE; [2] Neuroscience Department, College of Applied Medical Sciences, Imam Abdulrahman bin Faisal University, Jubail, Saudi Arabia; [3]John Walton Muscular Dystrophy Research Centre, Newcastle upon Tyne, UK; [4]Faculty of Medicine, University of Khartoum, Khartoum, Sudan; [5]Neurology Unit, Gaafar Ibn Auf Children's Specialized Hospital, Khartoum, Sudan

Objective: Focal seizures refer to the electrical and clinical manifestations of seizures that arise from one portion of the brain. The electroencephalogram (EEG) typically indicates a localized discharge over the area of onset. The objective of this study is to know the clinical profile and possible underlying causes of focal epileptic seizures among Sudanese children.

Methods: A cross sectional prospective hospital-based study was conducted at neurology out patients clinics from February 2014 to February 2015 on 86 patients with clinical diagnosis of focal epileptic seizures aged from 3 months to 18 years. A designed questionnaire has been administered and it includes detailed history, examination and investigations. Treatment type and short term effects were reported.

Results: Right sided focal motor seizures were the most common presentation. Neurological examinations correlate with seizure laterality. Seizure types were simple partial seizures (36%), complex partial seizures (37.2%), simple partial seizures evolving to generalized (10.5%) and complex partial seizures evolving to generalized (16.3%). Focal epileptic seizure types were Benign Epilepsy of Childhood with Centrotemporal Spikes (35.5%), frontal lobe epilepsy (24.4%), childhood epilepsy with occipital paroxysm (6.66%), multi focal seizures (6.66%) and parietal focal seizures (4.44%) in addition to others (22.22%). The correlation between seizure semiology and EEG findings was found to be of no statistical significance (p value .280). The underlying causes of focal epilepsy according to brain image findings were idiopathic in (42.9%), symptomatic in (57.1%), of which (34%) had brain atrophy, (27.3%) had vascular thrombosis and ischemic encephalopathy, (11.4%) had meningoencephalitis, (4.5%) had neurocutaneous syndrome, in addition to others. Full response to treatment occurred in (39.5%), decrease in frequency and duration of seizures occurred in (40.7%) while (17.4%) showed no response to treatment.

Conclusions: The most common type of focal seizures is complex partial seizures and most of the seizures were temporal in origin. EEG yield need more trained personnel in pediatric EEG.

Poster No. 220

Association between iron deficiency anemia and febrile seizures: a case-control study

S GIRI, DK DASH, SK BISOI, MD MOHANTY, SK PARIDA
Paediatrics, IMS & SUM Hospital, Odisha, India

Introduction: The association between iron deficiency anemia and febrile seizures is inconclusive due to inconsistent results reported in various previous studies. Low serum ferritin levels have been shown to reduce the seizure threshold. So, we conducted this case control study to determine any association between iron deficiency anemia and febrile seizure.

Materials and Methods: This case-control study evaluated 90 children aged 6 to 60 months in two 45 person groups taking fever with seizure as case and fever without seizure as control. The study was conducted in the Department of Paediatrics, IMS & SUM Hospital Bhubaneswar from January 2019 to June 2019. Diagnosis of iron deficiency anemia was based on CBC, serum iron, TIBC and serum transferrin level which was done for all participants.

Results: Girls were found to be more common in group with febrile seizure (75.5%) as compared to control group (42.2%). Viral fever was the most common cause of fever in the group with febrile seizure (51.1%) whereas acute gastroenteritis was the most common cause of fever in the control group (46.46%). The presence of iron deficiency anemia was 64.4% in the fever with seizure group as compared to 28.8% in the group with fever without seizure. The Chi Square test indicated a significant difference between two groups with a p value=0.0007 (p value <0.05 =significant).

Conclusions: The findings suggest that majority of children having febrile seizure suffer from iron-deficiency anemia and low serum iron which indicated that low serum iron and presence of anemia can serve as a trigger for febrile seizure.

Poster No. 221

Snakebite - a neglected menace: A prospective observational study in a tertiary care paediatric intensive care unit

S GIRI, DK DASH, SK BISOI, MD MOHANTY, SK PARIDA
Paediatrics, IMS & SUM Hospital, Odisha, India

Introduction: Snake envenomation is a well-known cause of morbidity and mortality in India. In 2009, WHO declared snake bite a neglected disease. Ophitoxaemia is an exotic term characterising the clinical spectrum of snake bite.
Objectives: (1) To study clinical profile, complications and outcome in pediatric cases of snake bite with special reference to envenomation time. (2) To highlight the atypical presentations of snake bite.
Materials and Methods: A prospective observational study was done in Paediatric Intensive Care Unit of our Hospital from June 2017 to June 2019.
Results: Around 56.8% of 109 cases were non-poisonous snakebites. Out of 47 cases admitted to PICU, 68.08% developed cellulitis at the site of bite with staphyloccoccus aureus being the commonest organism isolated (56.25%). Anaerobes (bacteroides and clostridium) were also isolated in few cases. Edema at site of bite (hematotoxic) and ptosis (neurotoxic) were most common initial presentation. 36.17% of patients received ASV and first aid within 6 hours of snakebite. The morbidity and mortality was significantly less ($p<0.05$) as compared to those who hadn't received ASV. 12.76% of cases with normal CRT presented with features of coagulopathy. DIC (58.33% of hematotoxic bites) and respiratory paralysis (68.75% of neurotoxic bites) were the commonest complications. Renal replacement therapy was required in 6.38%, transfusion in 10.63% cases and case-fatality-rate was 12.7%. There were a few atypical presentations of snakebite mimicking Gullain-Barre syndrome, acute onset encephalitis with absent brainstem and pupillary reflexes, intracerebral hemorrhage and cortical blindness.
Conclusion: Most snakebites are non-poisonous. One should not panic and over-treat since complications due to ASV are more. Early first aid and ASV administration has better outcome. Fibrinogen levels are more reliable than CRT to diagnose coagulopathy. Acute onset of atypical presentation i.e. altered sensorium, paralysis, blindness and stroke like features should always be evaluated for snake envenomation in suspected cases to prevent morbidity and mortality.

Poster No. 222

Infantile spasms?

M SAW[1], K LINN[1], HW AUNG[1], A AYE[1], C HLAING[1], A SAAN[1], K KO[1], M SWE[1], N LIN[1], P AUNG[1], W TUN[2]
[1]Pediatric Neurology Unit, Yangon Children Hospital, Yangon, Myanmar; [2]Pinlon Hospital, Yangon, Myanmar

[This abstract has been selected for oral presentation at Video Challenge session, when a panel of experts will attempt to make a diagnosis based on the case presented.]

Poster No. 223

Anti-MOG antibody associated demyelination masquerading as COVID-19 encephalopathy?

P ATHANASOPOULOS, K VRAKA, E HASSAN, D RAM, S WEST, H J TAN
Paediatric Neurology Department, Royal Manchester Children's Hospital, Manchester, UK

Introduction: Acute disseminated encephalomyelitis (ADEM) is a rare autoimmune disease involving inflammation of the brain and spinal cord, usually triggered by a preceding illness or vaccination. We describe a case triggered by SARSCoV-2.
Case: A previously healthy 1 year old girl presented with reduced GCS, decorticate posturing, seizures and a 3-day history of fever. She required intubation, was started on intravenous antibiotics, Aciclovir and Levetiracetam and was transferred to PICU. PCR nasal swabs revealed the child was SARSCoV-2 and Adenovirus positive. CSF investigations were normal, including a negative SARSCoV-2 RNA. MRI brain showed bilateral widespread T2 and FLAIR signal changes of subcortical white matter and the splenium. Diffusion restriction with T2/FLAIR signal change was noted in the thalami and pons. This was initially felt to be in keeping with Covid-19 encephalopathy, especially given the presence of the splenial lesion. A spinal MR was normal. She made good progress with steroid therapy and at discharge, was able walk a few steps, recognise voices, clap at nursery rhymes, eat and drink normally, but had cortical visual impairment, which is improving. Her anti-MOG antibodies were later found to be positive, which explains the symmetrical scan changes and brainstem involvement.
Discussion: In literature, there is a paucity of information regarding COVID-19 related encephalopathy. Lesions in the splenium of the corpus callosum appear to be a relatively consistent finding in children with PIMS-TS. Our child did not have any feature to suggest PIMS-TS. It is likely that SARSCoV-2 triggered off an inflammatory process in this child mediated by MOG antibodies.
Conclusion: In the advent of the COVID-19 pandemic, it is important not to attribute clinical findings to SARSCov-2 without excluding other disorders. MOG antibody associated demyelination may mimic the findings described in COVID-19 encephalopathy.

Poster No. 224

CSF pleocytosis as a prognostic marker in atypical meningitis – a child with mycoplasma meningitis and slow recovery

K SHETYE[1], N MOHAMED[1], P HARIJAN[2], J WHITEHORN[2], R RAMASWAMY[1]
[1]Peterborough City Hospital, North West Anglia NHS foundation Trust, Peterborough, UK; [2]Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

Background: Mycoplasma pneumoniae is increasingly recognised as an important cause of paediatric meningitis. We describe a child presenting with mycoplasma meningitis with an unusually severe CSF lymphocytosis and clinical course.
Case presentation: A 32-month-old girl with unremarkable birth and development, complained of sudden onset headache with fever, followed by unsteady gait, jerky eye movements and blurred vision. Examination showed an ataxic gait and horizontal nystagmus. MRI showed only prominent cerebellar foliae. Gradually,

she became more ataxic, unable to sit, non-verbal, and irritable with intermittent fever. She was treated with Ceftriaxone, Acyclovir and Clarithromycin. CSF revealed marked pleocytosis (444/μl WBC), with 90% lymphocytes, RBC 70/μl with raised proteins (0.7g/l) and low glucose (2.6mmol/l). Oligoclonal bands were negative. CSF culture, and extended viral PCR were negative. Seven days later repeat CSF showed 62 lymphocytes, 4 polymorphs, 6 RBC's, no organisms, normal flow cytometry, protein 0.34, glucose 3.5, and negative TB culture and 16SPCR. Mycoplasma titre was raised at 640 rising to 1280. Nasopharyngeal aspirate was positive for enterovirus and parainfluenza. Blood was normal for TFT's, amino acids, acylcarnitine, ANA, ANCA, aquaporin 4, serology (including brucella and retrovirus). Urine VMA and HVA, chest Xray and abdominal ultrasound were normal. Repeat imaging and genetic investigations are pending. Over the subsequent days her condition improved. Eight months later, she is alert, oriented, standing with support, has an age-appropriate vocabulary but remains ataxic and dysarthric. This child had a marked CSF lymphocytosis in the context of mycoplasma meningitis, in the absence of other causes of this. She developed a prolonged neurological deficit. We postulate that the adverse neurological outcome may be related to the extent of infiltration of the subarachnoid space by lymphocytes. This may be helpful in treatment decisions like considering the evidence for steroids in meningitis and in predicting the need for neurorehabilitation.

Poster No. 225
The use of cannabidiol in FIRES

M TAYLOR, S ALI, K PYSDEN, S HUSSAIN
Department of Paediatric Neurology, Leeds Children's Hospital, Leeds, UK

Objective: To describe the use of cannabidiol in a patient who had a pharmacoresistant epilepsy
Methods: Retrospective review of patient notes, neurophysiological data and pharmacological data.
Results: A previously well 15 year old girl presented with new onset convulsive seizures in association with a non-specific febrile illness. She remained refractory to emergency status management and was admitted to PICU for management with midazolam and thiopentone but failed to achieve any control of clinical and subclinical seizures. She was trialled on Levetiracetam, Phenytoin, Phenobarbitone, Clobazam, Lacosamide and Carbamazepine. The ketogenic diet was employed early in the course but also failed to achieve adequate ketosis or seizure control. Extensive investigations looking at infective, structural and metabolic causes failed to find an aetiology. Autoimmune encephalitis as well as treatment of a cytokine storm was considered and empirically treated with methylprednisolone, immunoglobulins, Anakinra and Tocilizumab. After remaining in refractory status for almost 6 weeks, a therapeutic trial of intravenous brivaracetam was commenced with a cessation of seizures within 24 hours. In the recovery period daily seizures remained problematic and were associated with respiratory arrest and profound desaturation. Further drugs utilised included sodium valproate, oral phenytoin and oxcarbazepine. Despite these interventions seizures were increasing and were hampering the cognitive improvements made. Cannabidiol was introduced (and escalated to 7mg/kg/day) as there was a degree of evidence in the literature with seven patients described in a single case series.
Conclusions: Our patient remained in refractory status epilepticus until treatment with brivaracetam was introduced. The introduction of cannabidiol at a modest dose of 7mg/kg/day has reduced seizure frequency from daily to once every 1 or 2 months. This case adds more evidence for the use of cannabidiol in FIRES.

Poster No. 226
Leukoencephalopathy with Bright Tree Appearance

A YAWORSKI, N LIU, J MAILO, J KASSIRI
Pediatric Neurology, University of Alberta, Canada

Objectives: Acute encephalopathy with biphasic seizures and delayed diffusion restriction (AESD) is one of the most common pediatric encephalopathies described in Japan, but has not been reported in Canada. AESD is diagnosed clinically and is characterized by biphasic seizures and diffusion restriction in a bright tree appearance (BTA) on neuroimaging and overall has a low mortality rate. Our objective was to identify cases within our Canadian centre.
Method: Pediatric neurology patients under age 18 years with a diagnoses of AESD were retrospectively reviewed between January 2019 and January 2020 at the Stollery Children's Hospital in Edmonton, Canada. This was a retrospective ethics approved (ethics Pro00099091) study.
Results: In this case series we present 3 different patients diagnosed with AESD based on clinical presentation and imaging findings. This included a 22 month old Caucasian girl, a 4 year old Filipino girl and a 3 year old Caucasian boy. Two patients had a preceding respiratory infection with enterovirus, while the third patient had no infection isolated. Vitamin B6 was used in 2 patients and L-carnitine used in the third. Two patients received high-dose steroids, and one received consecutive plasma exchange therapy. One patient's case resulted in death while the remaining two had significant morbidities and one developed post encephalopathic epilepsy
Conclusion: This case series identifies that AESD is a cause of acute encephalopathy in North America and should be considered in patients of any ethnicity presenting with febrile status epilepticus, elevated liver enzymes, abnormal EEGs and prolonged waking period. There is very little research on AESD from North America, and what is available is case studies. More research is needed on the natural evolution of AESD cases, biomarkers to differentiate from febrile status epilepticus, and further management options.

Poster No. 227
Cerebral venous thrombosis complicating acute mastoiditis

KL STEVENSON, N HOPE, K TRIMBLE, D PEAKE
Royal Belfast Hospital for Sick Children, Belfast, UK

Objective: Acute otitis media (AOM) is common, having affected up to 84% of 3 year-olds. Acute mastoiditis (AM) is the most common complication of AOM affecting the paediatric population with an estimated incidence between 1.2 and 4.2/100,000 children/year. Cerebral venous thrombosis (CVT) is a rare complication of AM with management approaches varying between clinicians. This case review was designed to evaluate the recent experience with cerebral venous thrombosis in AM at a tertiary paediatric centre with a view to guideline development.

Methods: A list of patients admitted with acute mastoiditis from February 2019 to February 2020 was retrieved from the coding department. A case note review of these children was performed.
Results: 10 children were admitted with AM. 3 (33%) were found to have CVT. All 3 (100%) underwent cortical mastoidectomy with ventilator tube insertion. Two cases (67%) cultured Fusobacterium necrophorum in keeping with Lemierre's syndrome. The sigmoid sinus was universally affected in our cohort. Two (67%) were anti-coagulated due to signs of raised intracranial pressure. Both children were given LMWH, however one child was initially commenced on unfractionated heparin. One child (33%) developed carotid artery occlusion, frontal lobe infarcts and required acetazolomide for raised ICP. One (33%) received seizure prophylaxis. At 3 months follow-up imaging, 3 patients (100%) had improved sinus flow, 1 (33%) had complete radiological resolution. 1 child (33%) had ongoing neck stiffness, otherwise complete clinical otoneurological recovery was noted.
Conclusion: Despite a small cohort, there appears to have been a higher rate of CVT secondary to mastoiditis in our case series (30%) than seen elsewhere. A watchful eye must be maintained to detect a trend in the future. Management strategies were diverse and a Trust wide guideline to direct management in these cases would be of benefit to paediatric neurologists, otolaryngologists and infectious diseases alike.

Poster No. 228
A case series of infants with cytomegalovirus infection in Indonesia: various clinical and radiographic manifestations

A ASWIN[1], MRS MUHYI[2]
[1]*Faculty of Medicine, Mulawarman University, Samarinda, Indonesia;*
[2]*Department of Child Health, Mulawarman University/RSUD Abdul Wahab Sjahranie, Samarinda, Indonesia*

Objective: Cytomegalovirus (CMV) is a DNA virus that affects the central nervous system. Congenital CMV infection incidence in developing countries is between 1 and 5% of all live births. The most commonly observed physical findings are petechial rash, jaundice, and hepatosplenomegaly with neurologic abnormalities such as microcephaly and lethargy.
Methods: The data of patients with CMV who followed-up between December 2019 and January 2020, three patients were retrospectively reviewed.
Results: We identified three infants diagnosed with CMV infection with ages ranged between 2 months and 7 months. All patients presented with seizure without febrile and required admission to PICU for respiratory compromise due to status epilepticus. One patient had microcephaly and one other patient had lethargy and a history of neonatal jaundice. None of them had petechial rash or hepatosplenomegaly. Two patients were confirmed with pneumonia by physical examination and chest x-ray. CT head in the first patient showed impaired brain development on the frontal lobe. CT head in the third patient showed cerebral atrophy. Echocardiography on the second patient showed heart abnormalities, with perimembranous ventricular septal defect and secundum atrial septal defect. The diagnosis of all patients were confirmed by viral DNA detection and serologic tests. To confirm a diagnosis of congenital or perinatal infection was not possible due to the absence of testing within the first 2 weeks of life. All patients received intravenous ganciclovir for 6 weeks, phenytoin, and phenobarbital.
Conclusion: We hereby present cytomegalovirus infection in infants diagnosed by viral DNA and serological test. Our case series showed infants with CMV infection, seizures were the most common clinical feature, and admission to PICU was needed. The abnormal findings on CT head and echocardiography were found. However, CMV is associated with severe neurological conditions, early support needs to be provided.

Poster No. 229
Acute encephalopathy in a child with OTC deficiency despite normal ammonia levels responsive to plasmapheresis

D BASKARAN[1], I RONCERO[1], M ANDERSON[2]
[1]*Paediatric Neurology, Great North Children Hospital, Newcastle upon Tyne, UK;*
[2]*Paediatric Metabolic medicine, Great North Children Hospital, Newcastle upon Tyne, UK*

Introduction: Ornithine transcarbamylase (OTC) deficiency is the most common urea cycle disorder. Affected individuals are prone to episodes of encephalopathy associated with hyperammonemia. We report a case of OTC deficiency presenting with acute encephalopathy despite normal ammonia levels who responded to plasmapheresis.
Case report: A 9 year boy with known OTC deficiency presented with acute onset of focal seizures and a movement disorder. On examination he had mild left hemiparesis, dysarthria and chorea. Bloods including ammonia and amino acids profile were normal. Head MRI revealed bifrontal gliosis from previous episodes of hyperammonemia. He received intravenous scavengers with little improvement. His seizures progressed to an epileptic encephalopathy despite multiple anticonvulsants. A repeat MRI revealed generalized cortical changes suggestive of cerebral edema. CSF amino acids were normal. MRSpectroscopy (MRS) done was later reported to show glutamine and glycine peaks. In view of worsening symptoms auto-immune encephalitis was considered. Accordingly he was investigated and treated with pulse intravenous methylprednisolone for 5 days and IVIG 2g/kg. Despite improved seizure control, there was no improvement in his movement disorder and his encephalopathy. A third MRI did not show any new changes and the decision was made to start plasmapheresis. After the first session there was a clear improvement that was sustained over 5 sessions in total. He was discharged 1 month after admission being almost completely back to his normal self. Investigations for auto-immune encephalitis were all negative. The response to plasmapheresis and the MRS findings made us attribute the child's presentation to his OTC deficiency.
Conclusion: We should consider OTC encephalopathy in OTC deficient patients despite normal ammonia levels. The MRS showing peaks of glutamine can help with the diagnosis as amino acids profile can be normal in blood and CSF. Plasmapheresis led to resolution of encephalopathy in our patient.

Poster No. 230

Neurological deficit following Dinutuximab infusion

R SMITH[1], M HANSON[2], J TURNBULL[3], G CHOW[1]

[1]Department of Paediatric Neurology, Queen's Medical Centre, Nottingham, UK; [2]School of Medicine, University of Nottingham, Nottingham, UK; [3]Department of Paediatric Oncology, Queen's Medical Centre, Nottingham, UK

Background: Dinutuximab is a chimeric monoclonal antibody which targets GD2 (glycolipid disialoganglioside), an antibody which is minimally expressed on normal human neurons, but highly expressed on neuroectodermal tumours, particularly neuroblastoma. Dinutuximab induces cell lysis via antibody-dependent cellular cytotoxicity. There is an uncommon but potentially serious risk of neurotoxicity.

Case report: We report the case of a 5 year old girl who presented with abdominal pain and was found to have a paraspinal mass on ultrasound, identified as a neuroblastoma. Tumour genetics demonstrated segmental chromosomal abnormalities including loss of 11q and gain of 17q (MYC N was not amplified). Following high risk classification, the patient underwent complete surgical resection, also receiving high dose chemotherapy with stem cell rescue, and focal radiotherapy. This was followed by the immunotherapy phase. However, on approximately Day 8 of Dinutuximab infusion, the patient began experiencing an evolving weakness with loss of proprioception particularly in the lower limbs, as well as dilated pupils, difficulty with fine motor movements, and significant hypertension and tachycardia. MRI demonstrated thickened and enhancing cauda equina nerve roots, in keeping with an acute inflammatory polyneuropathy. Nerve conduction studies demonstrated evidence of sensory axonal peripheral polyneuropathy. Dinutuximab therapy was discontinued. She was managed with two courses of IV immunoglobulin treatment over 2 months as well as a course of oral steroids. She made a full recovery over months, but has persistent hypertension and tachycardia, and remains on a beta-blocker.

Conclusion: Glycolipid GD2, although a target for the treatment of neuroblastoma, is also found on the surface of neurones and peripheral sensory fibres. Dinutuximab therefore has the potential to cause neuronal damage resulting in peripheral neuropathy and neuropathic pain. Severe neuropathic pain occurs in more than 50% of patients receiving the drug, and motor/sensory neuropathy in between 1 and 9%. This adverse effect remains under national monitoring.

Poster No. 231

Out of Sight: Retrobulbar optic neuritis

E YU, S NICOL, T SMITH, D RAM

Department of Paediatric Neurology, Royal Manchester Children's Hospital, Manchester, UK

Introduction: Optic neuritis in children classically presents with papillitis, alerting the clinician to the diagnosis. We present a case of anti-MOG antibody associated retrobulbar optic neuritis with a delayed diagnosis due to normal ophthalmological findings.

Case: Our patient is an 8 year old previously well boy who woke up with acute bilateral visual blurring. He had painful eye movements which resolved within a few hours. A standard MR brain and detailed ophthalmology assessments were normal. His neurological examination was unremarkable and he was discharged by the local paediatric team with suspected functional visual loss. He re-presented 1 week later with more significant visual loss, having only light perception at this stage. Repeat ophthalmological findings were normal but he had delayed visual evoked potentials bilaterally, suggesting optic neuropathy. An urgent MR scan with contrast demonstrated prechiasmatic enhancement of both optic nerves, confirming retrobulbar optic neuritis. His MR brain and spine were unremarkable otherwise and CSF oligoclonal bands were negative. Anti-MOG antibodies were positive and he made a full recovery with steroid therapy, taking 8 weeks to regain normal visual acuity.

Discussion: Paediatric optic neuritis typically presents with visual loss associated with disc oedema (papillitis), which aids rapid diagnosis. Loss of colour vision and painful eye movements are not always reported in younger children. Retrobulbar optic neuritis rarely occurs in children, and optic discs appear normal in these patients. Orbital MRI with post-contrast sequences demonstrates retrobulbar nerve enhancement. Anti-MOG antibodies are known to be associated with retrobulbar neuritis, and patients respond particularly well to steroids. An early diagnosis therefore enables swift administration of treatment.

Conclusion: In children with acute visual loss, optic neuritis should always be considered even in the absence of ophthalmological findings to suggest this. Orbital MRI with post-contrast sequences should be performed in these children to help aid diagnosis.

Poster No. 232

An inflammatory myositis secondary to anti-retroviral therapy in a child; case report and review of the literature

M MONAGHAN[1], C LOH[1], A OWARE[3], K URANKAR[4], M RODERICK[2], A MAJUMDAR[1]

[1]Department of Paediatric Neurology, Bristol Royal Hospital for Children, Bristol, UK; [2]Department of Paediatric Immunology, Bristol Royal Hospital for Children, Bristol, UK; [3]Department of Neurophysiology, University Hospitals Bristol NHS Foundation Trust, Bristol, UK; [4]Department of Neuropathology, Southmead Hospital, Bristol, UK

We describe the presentation and follow-up of an HIV positive 5 year old girl who had a 6-week onset of rapidly deteriorating mobility, progressive proximal muscle weakness and a raised Creatine Kinase (CK) of 4330U/L diagnosed with inflammatory myositis. Potential causes were investigated by paediatric Neurology and Immunology teams. Her viral load had been undetectable over the preceding 2 years, excluding an HIV myositis. An MRI showed no definite myositis. A muscle biopsy showed evidence of an inflammatory process, comprising a moderate endomysial, perimysial and perivascular mononuclear (CD8+T cell) infiltrate with increased MHC expression. No particular features of dermatomyositis or immune-mediated necrotising myopathy were identified and there were no features of an inclusion body myositis. Regarding causes, anti-retroviral medications were considered. She had had a recent switch in medication, from twice daily Raltegravir (an Integrase Strand Transfer Inhibitor, INSTI) to once daily Dolutegravir (an INSTI) while continuing on established daily Abacavir and Lamivudine (Nucleoside Reverse Transcriptase Inhibitors). Dolutegravir is not cited as a cause of inflammatory myositis and in one study was not associated in the adult population with a risk of significant CK level rise. It is known that other anti-retroviral medications, such as Zidovudine and Lamivudine, may cause this potential adverse effect. Changing the Dolutegravir back to Raltegravir, in

combination with continuing Lamivudine and Abacavir made no difference to her weakness. These drugs had been well-tolerated over the preceding 7 month period. Changing the anti-retroviral regime completely to monotherapy with Ritonavir and Darunavir (Protease Inhibitors) resulted in a dramatic improvement. Within 10 days she regained the ability to stand and walk, with a concomitant reduction in her CK from 1700 at time of switch to 403U/L. This case highlights the potential risk of developing inflammatory myositis from anti-retrovirals even years into treatment.

Poster No. 233

Management of infratentorial subdural empyema in infants - is neurosurgical intervention always necessary?

MA YARAGATTI, R ADIGA
Rainbow Children's Hospital, Bangalore, India

Objectives: Infratentorial Subdural Empyema in infants and children is rare and life-threatening complication of bacterial meningitis. Controversy regarding the best management attests to the poor outcome of this intracranial infection. We report an infant with complicated meningitis, ventriculitis with subdural empyema who was managed conservatively with good outcome.
Methods: Review of case notes and literature.
Results: 29-day old infant with normal antenatal history, full term normal delivery on exclusive breast feeding presented with 3-day history of fever, irritability, and one episode of seizure. Systemic examination was normal other than being febrile and irritable. Investigations revealed elevated CRP and PCT, CSF analysis showed high protein, low sugars and increased cell count with neutrophilic predominance. She was started on intravenous ceftriaxone which was changed to meropenem and amikacin as blood and CSF cultures yielded ESBL E. coli. On day 8 of illness in view of persistent fever, MRI brain was done which revealed subdural empyema along the left temporal area and bilateral suboccipital/cerebellar convexity with features of ventriculitis. Since baby was clinically better, after multidisciplinary discussion we planned neurosurgical intervention only if there was clinical deterioration. Piptazobactam and prophylactic levetiracetam were started. Antibiotics were continued for a total of 6 weeks. MRI Brain on day 18 of illness showed reduction; MRI Brain showed complete resolution of empyema and ventriculitis after 6 weeks of intravenous antibiotics. On follow up, baby has normal development with no neurological deficits.
Conclusion: This infant with subdural empyema showed an excellent response to a long course of appropriate antibiotics. This case illustrates that children with subdural empyema may be managed conservatively however should be monitored closely for clinical deterioration and with serial MRI Brain scans. Neurosurgical intervention may not always be necessary.

Poster No. 234

A rare presentation of central pontine myelinolysis (Osmotic Demyelination Syndrome) associated with refeeding syndrome

D BASKARAN[1], RJ FORSYTH[1], KK PANG[1], D MITRA[2], J TAN[3]
[1]Paediatric Neurology, Great North Children's Hospital, Newcastle upon Tyne, UK; [2]Neuroradiology, Royal Victoria Infirmary, Newcastle upon Tyne, UK; [3]Royal Manchester Children's Hospital, Manchester, UK

Introduction: Paediatric osmotic demyelination syndrome (ODS) is a rare condition and a recent review identified 106 paediatric cases between 1960 and 2018. ODS in adults is associated with chronic alcoholism, rapid correction of hyponatremia and liver transplantation. We report a case of central pontine myelinolysis despite appropriate correction of severe hyponatremia.
Case report: A 15 year old girl with ulcerative colitis (UC), on Azathioprine, was admitted in a confused and agitated state with minimal communication. She was severely malnourished and dehydrated in shock needing fluid resuscitation. She had deranged renal function and a very low sodium of 115mmol/L. CT Brain was normal. In the preceding 5 weeks she had adopted an extremely restricted vegan diet leading to 7kg weight loss. Her acute confusional state was attributed to hyponatraemia and possible Wernicke encephalopathy. Despite sodium correction at recommended rate she sustained central pontine myelinolysis (CPM) - MRI demonstrated patchy T2 signal changes in pons with associated restricted diffusion in central pons. Typically, she had an initial milder phase but subsequently developed severe pseudobulbar palsy associated trismus which affected her expressive communication/oral intake and pseudobulbar affect with emotional lability. She had symmetrical limb movements but could not hold head or sit. She remarkably improved over the subsequent 6 weeks - began to walk unaided, talk and feed orally. She had hepatitis and multiple electrolyte disturbances due to refeeding syndrome which was the likely cause of CPM
Discussion: Disruption of the blood-brain barrier is thought to have an important role in the pathogenesis of ODS and it is usually seen in areas with maximum admixture of grey and white matter. Seizures, ophthalmoplegia, quadriparesis, 'locked-in' syndrome and in severe cases death can also occur with ODS. Current management of ODS in children is supportive, with potential benefit from steroids and dopaminergic drugs.

Poster No. 235

Relapsed Herpes simplex encephalitis: case report and literature review

C TAN, D NAGA, U VARMA
Royal Manchester Children's Hospital, Manchester, UK

Background: Herpes simplex virus (HSV) type 1 encephalitis is one of the most common causes of sporadic encephalitis with annual incidence of 1 in 250000 to 500000. Recurrence is rare with majority of them being within months of first presentation. We present a rare case of recurrence 12 years after the initial presentation and look at the literature of paediatric relapsed HSV encephalitis.
Case: A 12-year-old girl presented with prolonged seizures following 2 days of fever and vomiting. Her past history included HSV encephalitis at the age of 4 weeks when she presented with

seizures. She had negative CSF HSV PCR but positive blood HSV PCR and MRI brain changes consistent with diagnosis of HSV encephalitis. After 3 weeks of IV acyclovir and a negative HSV blood PCR, the treatment was stopped. She developed epilepsy and left hemiparesis as a sequel. She was on levetiracetam which was weaned 10 months prior to this new presentation. For this presentation 12 years later, she was commenced on antibiotics and acyclovir. MRI brain revealed new areas of abnormality consistent with the pattern of acute HSV encephalitis along with the old changes. Lumbar puncture (LP) performed showed HSV DNA type 1 PCR in CSF. A repeat LP performed 3 weeks after treatment with acyclovir showed negative HSV PCR. She is back to her baseline with no new deficits following her relapse.
Discussion: HSV encephalitis needs to be considered in any patient presenting with fever and seizures. Reactivation of the virus in neurological tissue and genetic susceptibility has been proposed as a mechanism in relapse. Prolonged treatment with IV acyclovir has reduced the rates of relapse. A repeat LP before stopping acyclovir should be considered. The evidence for prophylactic acyclovir to prevent relapse is lacking.

Poster No. 236
Delayed onset of neurological symptoms after infant TBI: Challenges for treatment

T LAZARUS[1,2], GT LAZARUS[2]
[1]Private Practice, Durban, South Africa; [2]Department of Psychology, Emory University, Atlanta, GA, USA

Objective: To discuss delayed onset of symptoms in TBI in very young infants.
Methods: Case conceptualization and discussion of infant TBI. Following her involvement in a motor vehicle accident at the age of 2.5 months, a young infant initially presented as stable, alert and playful, with no open injuries on examination. Five months thereafter, she presented again at hospital with a history of vomiting, fever, rigors, crying and irritability, and fitting. She was given multiple doses of both Valium and a Phenytoin infusion for seizure control.
Results: She was dull and floppy with sunken fontanelle and had increased tone, on the right side. CT brain scans revealed bilateral chronic subdural collections that were greater on the left side, associated with minimal midline shift and subdural collection suggestive of an old haematoma. She was treated conservatively with antibiotic treatment and neurological monitoring and despite showing progress in neurological parameters, had persisting signs of increased tone and reduced movement on the right side, suggestive of a right hemiparesis. Neuropsychological assessment conducted 12 months post-accident revealed severe language and symbolic play regression, emotional distress patterns that were particular in stranger situations, and disruptive sleep patterns (reported by mother). Play therapy involving mother and therapist revealed an erratic progression and rapport was difficult to maintain over sustained periods. Patient had deficits in sustained attention and postural control maintenance during active and directed play which contributed to her slow progress in rehabilitation. Patient was considered for small doses of stimulant medication by a pediatric neurologist to improve attention, although concerns about stimulant medication use in traumatic brain injuries with intracranial haematoma in infants posed a serious concern. Behavioural management was considered.
Conclusions: The impact of severe head injuries on young infants in countries with developing populations and challenges for early treatment and rehabilitation are discussed.

Poster No. 237
Posterior reversible encephalopathy syndrome unveiling post streptococcal glomerulonephritis

AD HOLT, R EVANS, S SASTRY
New Cross Hospital, Wolverhampton, UK

A 10 year old girl presented with a 1 day history of headaches, vomiting and confusion. She developed vacant episodes and progressed to generalised tonic-clonic seizures which were terminated by intravenous Lorazepam and Levetiracetam. MRI brain was performed on the day of admission and showed features consistent with Posterior Reversible Encephalopathy Syndrome including T2 hyperintensity and mild acute diffusion restriction extending along the parieto-occipital subcortical white matter and temporal lobes bilaterally, with a further focus also seen in the right frontal lobe. Blood pressure recordings were above the 95th centile and she was transferred to a local Paediatric Intensive Care Unit for anti-hypertensive therapy including Furosemide and Nifedipine. Magnesium, lactate dehydrogenase, urea and creatinine were elevated. Serum complement levels were low. Urinalysis showed blood and protein. Renal Ultrasound identified cortical enhancement in keeping with glomerulonephritis and ASOT was significantly elevated (3500). She was treated with intravenous Phenoxymethylpenicillin for a previously unidentified post streptococcal glomerulonephritis. MRI changes had resolved on repeat neuroimaging 4 weeks later. Vacant episodes persisted for the next few weeks, although she went on to remain seizure-free for the subsequent several months and anti-epileptics were weaned off and stopped. There was some persisting hypersomnolence, with sleep studies within normal limits suggesting post encephalopathy recovery rather than any other pathology. She continued to improve and was weaned off anti-hypertensive medication 5 months after her initial presentation. The above case featured a patient with hypertension and seizures, in the absence of oedema, oliguria or frank haematuria. Early recognition neuroimaging aided a prompt diagnosis and enabled the relevant management to be commenced in the appropriate critical care setting.

Poster No. 238
Viral and bacterial encephalitis in children: A case series report

R PERDANI[1], D PURNAMA[2]
[1]Pediatric Department of Medical faculty of Lampung University, Indonesia; [2]Medical Faculty of Lampung University, Indonesia

Background: Viral and bacterial encephalitis in children has a higher incidence than other infections of the central nervous system. The mortality, morbidity and scalding rates after infection are very high. The complications that arise can affect the development of the child.

Objective: It was a case-series which was objected to differentiate between bacterial and viral infection of central nervous system (CNS).
Results: The case presentation contained 3 cases of CNS infection, namely 2 viral infections and 1 bacterial infection. There were differences in term of history of the disease, the progression, and also the characteristic of the cerebrospinal fluid examination. Diagnosis was carried out by history, physical examination and investigation. There was difference in the results of the CSS examination compared to the theory. However, adequate treatment can be carried out against the suspected microorganisms. In addition, physiotherapy was carried out in further recovery. Of the three cases and due to limited facilities and infrastructure in determining the type of virus, the patient could be cured and could follow physiotherapy well.
Conclusions: The diagnosis of encephalitis were based on history, physical examination and laboratory investigation. Adequate treatment for patients might reduce the number of disabilities caused by the disease.

Poster No. 239
Management of a unique case of acute disseminated encephalomyelitis (ADEM) in a low-resource setting

SHUKLA[1,3], A PANDAY[3], P MAHARAJ[2], A MAHABIR[1], GGS SCANTLEBURY[1], I CUDJOE[1], A MOONA[4], DM BIRD[1], S LATCHMAN[1], L AKAN[1]
[1]*Paediatrics, Eric Williams Medical Sciences Complex, Trinidad & Tobago;* [2]*Radiology, Eric Williams Medical Sciences Complex, Trinidad & Tobago;* [3]*Neurology, Eric Williams Medical Sciences Complex, Trinidad & Tobago;* [4]*Neurophysiology, Eric Williams Medical Sciences Complex, Trinidad & Tobago*
Aim: We describe a unique case of ADEM with the probable viral aetiology being COVID-19.

Clinical findings: NC, a 20-month-old male presented in July 2020 with new-onset focal motor seizures, drowsiness and developmental regression. There was a preceding history of fever, vomiting and diarrhoea about 1 to 2 weeks prior to presenting. On examination, he was noted to have erythema nodosum over his shins, unable to fix and follow even to light stimulus, no head nor trunk control with generalized increased tone, hyperreflexia and upgoing plantar responses bilaterally.
Investigations: Blood investigations: lymphopenia, mild increase in ESR 16mm/hr, transaminases elevated, CK elevated. CSF investigations: CSF protein 143mg/dL, glucose 88mg/dL, CSF cell count 28 white cells, 17 red cells. EEG: background slowing right > left. MRI brain (initial): transient lesions along corpus callosum, petechial haemorrhages within superior aspect of cerebellar vermis
Treatment: He was treated with 5 days IV methylprednisolone 30mg/kg/day followed by oral prednisolone. He was treated as a protracted ADEM illness with IVIG (2g/kg over 2 days) when he clinically deteriorated. Steroids were slowly tapered over 8 weeks.
Progress: 2 weeks post IVIG - speech and language milestones improved to baseline, started cruising. 6 weeks post IVIG - able to walk independently however, not able to climb/run.
Follow-up investigations: 2 months post admission: 2019-CoV IgM Antibodies (blood): 1.123 (range 0–1). Of note, we have had a total of 4 patients managed for ADEM within the past 3 months. 3 presented with preceding viral GE symptoms. Most recently the other was initially managed for Kawasaki disease and is also COVID 19 IgM positive. We are awaiting COVID-19 antibody testing for these patients to determine whether they are linked. Unfortunately, in our resource-limited setting, PCR testing was initially only performed on patients with a travel history and respiratory symptoms.

Poster No. 240
Clinical characteristics and laboratory findings in patients with febrile seizures

A ASWIN[1], MRS MUHYI[2], MRS HASANAH[3]
[1]*Faculty of Medicine, Mulawarman University, Samarinda, Indonesia;* [2]*Department of Child Health, Mulawarman University/RSUD Abdul Wahab Sjahranie, Samarinda, Indonesia;* [3]*Department of Histology, Faculty of Medicine, Mulawarman University, Samarinda, Indonesia*

Objective: Febrile seizure is a convulsion disorder in children aged 6 months to 5 years that associated with a fever and present without any intracranial infection. In a study, 1 of 25 children in the population estimated to develop at least one febrile seizure in their childhood, and the most frequent etiology of febrile seizure was respiratory tract infection. There is growing literature on febrile seizures, but little is known about febrile seizures caused by respiratory tract infection.
Methods: Data were obtained from medical records in RSUD Abdul Wahab Sjahranie from 2016 to 2017 and showed 31 patients using purposive sampling that fulfilled the inclusion and exclusion criteria.
Results: From 31 patients showed there were 22 (71%) male patients and 9 (29%) female patients. Respondent age ranged from 0 to 60 months old with the most respondents ranged from 0 to 12 months (38.7%). Simple febrile seizures and complex febrile seizures were observed in 64.5% and 35.5% respectively with temperature was ranged 37-38.9 C (32.3%), and length of fever before hospitalized was 1 day (74.2%). The most frequent nutritional status was good (90.3%), birth weight >2500 gram (93.5%), normal vaginal delivery (80.6%), and no family history of seizure (54.8%). The laboratory test result showed the mean of erythrocyte, hemoglobin, hematocrit, MCV, MCH, MCHC, thrombocytes were in the normal range, and leukocytes were increased.
Conclusion: The febrile seizure caused by respiratory tract infection represents a cause for admission of children. In this study, the febrile seizure was observed predominantly in male, younger age, simple febrile seizure type, temperature range 37 to 38.9°C, length of fever 1 day, good nutritional status, normal birth weight, normal labor, and no family history of seizure. Respiratory tract infection as the underlying disease could conduct the result of leucocytosis.