Poster Presentations

Poster 001

Can social distancing and changes in health behaviours reduce infection-triggered neuroinflammation?

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Background: Many neuroinflammatory disorders including autoimmune and post-infectious encephalitis are observed to have a seasonal variation. We evaluated changes in the incidence of neuroinflammatory disorders in association with the COVID-19 pandemic, hypothesising that social distancing and changes in health behaviour would lead to a reduction in infection-triggered conditions.
Methods: In this single institution retrospective study, we reviewed all children admitted during the COVID-19 pandemic between March 2020 and March 2021, identifying those with new onset and non-COVID associated acute demyelinating syndrome (ADS), multiple sclerosis (MS), Guillain-Barre syndrome (GBS), autoimmune encephalitis (AE) and post-infectious encephalitis (PIE). Incidences were compared with the three years pre-pandemic (2017–2020). Two-tailed p-values were calculated from z-scores for 2020 to 2021 with respect to the 2017 to 2020 distributions.
Results: The number of children admitted with AE during the COVID-19 pandemic (2020–2021) was 3, compared to 7.67 (annual mean during 2017–2020) representing a 61% decline ($p<0.001$). PIE decreased by 30% from a mean of 10 to 7 ($p=0.26$). Whereas, GBS, ADS and MS were not statistically significant with 3, 6 and 10 admissions during the pandemic compared to a mean of 3.33, 8.33 and 9.33 admissions in 2017 to 2020, respectively.
Conclusion: The significant decrease in the incidence of AE during the COVID-19 pandemic suggests that disruptions to seasonal endemic infection transmission by changes in social mixing and health behaviours can modify the link between infection and autoimmune encephalitides. However, incidence of other neuroinflammatory conditions typically presumed to have an infectious trigger such as GBS and ADS was not reduced, suggesting infectious triggers may either be less important in the aetiology of these conditions or that this link is more complex and cannot be observed within the epoch of behavioural change. Autoimmune induction may indeed involve longer lags from infection, require a second infection and be influenced by other environmental and genetic factors.

Poster 002

Chickenpox and stroke – joining the dots

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Objective: Varicella zoster virus (VZV) causes many CNS complications. In the paediatric population it is a leading cause for CNS vasculopathy, mainly affecting the basal ganglia. There is a significant risk of morbidity including recurrent cerebrovascular events and persisting hemiplegia and hemidystonia. We aim to review regional recognition and management of this important but rare condition.
Methods: We performed a retrospective case review of all children diagnosed with varicella related stroke in the North East region of the UK between 2010 and 2020.
Results: 13 children were 'diagnosed' with VZV associated CNS vasculopathy. 12 presented with hemiparesis, 1 child with isolated slurred speech and all with classical MRI/MRA changes. All had a clinical history of chicken pox within 10 months, 1 was during acute infection. 8 children were confirmed blood VZV IgG positive. Only 4 had virological confirmation; 3 in CSF and 1 in blood. Of 9 lumbar punctures performed, 3 were VZV positive. Of 4 tested, none had intrathecal antibody production. All had prolonged anticoagulation with duration based on follow up MRI/MRA and varying short courses of antivirals and steroids. All fully recovered.
Conclusion: There are widely varying management strategies for VZV vasculopathy in children. Of 13 patients diagnosed, investigations were not complete in 8. We propose that children presenting with classical signs within 12 months of chicken pox have the following: MRI plus MRA, paired blood and CSF VZV IgG and PCRs alongside extended thrombophilia screening and echo. Treat with a 5 day course of oral prednisolone, 14 days of IV aciclovir and 12 months anticoagulation via aspirin with prolongation if residual vasculopathy on follow up MRA/MRI at 12 months. Increasing our knowledge and standardising investigations will increase our recognition of this condition.

Poster 003

Cryptococcus isolates from patients with or without immune reconstitution inflammatory syndrome have a different cell wall composition and induce different levels of TNF from bone marrow derived macrophages

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Background: Immune reconstitution inflammatory syndrome (IRIS), a major complication of cryptococcal meningitis, occurs after HIV-positive adults or children begin antiretroviral therapy. Current theory suggests a paucity of pro-inflammatory cytokines including tumour necrosis factor (TNF) at initial infection leads to persistent antigenaemia and uncontrolled inflammation on immune reconstitution. Little is known about the contribution of pathogen-associated factors.
Methods: Flow cytometry cell wall staining was used to compare Cryptococcus neoformans clinical isolates from patients who developed IRIS and those who did not using standard and 'host-mimicking' in vitro growth conditions. These isolates were then incubated with bone marrow derived macrophages (BMDMs) and TNF production measured as a model of innate immune activation, with the hypothesis that the differential cell surface composition of IRIS versus non-IRIS isolates may impact macrophage activation thresholds leading to differential TNF response.

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Results: Different in vitro growth methods led to differences in C. neoformans growth, morphology and cell wall composition. In host-mimicking media, IRIS isolates had significantly fewer cells stained for both chitin and chito-oligomers than non-IRIS isolates (54.3% [52.3, 55.9] vs 57.4% [53.0, 63.9]; p=0.05; median [IQR]) and stimulated BMDMs to release significantly less TNF after IL-17 priming (11.7ng/ml +/- 2.0 vs 3.4ng/ml +/- 1.0; p=0.001; mean +/- SEM).
Conclusion: Our results suggest that there are pathogen-related predisposing factors to IRIS development that need to be further elucidated to understand and prevent this fatal complication.

Poster 004
How does amplitude integrated electroencephalography influence the care of children on a paediatric critical care unit?

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Background: Accurate diagnosis of seizures in children on paediatric intensive care unit (PICU) is challenging due to paralysis and sedation. Continuous electroencephalogram (EEG) is the criterion standard investigation for diagnosing seizures but it is not available around the clock. Amplitude integrated electroencephalogram (aEEG) is a simplified and time compressed version of EEG, allowing non-specialists to analyse the trace.
Objective: This service evaluation evaluated the effectiveness of aEEG as a monitoring tool for seizures on PICU.
Methods: A retrospective case note review of children who had been monitored with aEEG whilst on PICU in Sheffield Children's NHS Foundation Trust between June 2019 and May 2021. Participant demographics were collected along with details about their stay on PICU were collected. The indication and any analysis of the aEEG was noted. The aEEG trace were analysed for comparison against the notes. The impact aEEG had on the management of the participant was assessed and categorised as helpful, not helpful, or borderline/unclear.
Results: 38 participants were part of this study, having 45 aEEG traces. It was most often used after a clinical seizure (38%). 10 (22%) displayed seizures. On 9 occasions the staff missed seizures on aEEG, 6 of which were smaller events of a single or multiple missed seizures, and 3 were status epilepticus. 45% of the participants had their management helped by aEEG, 16% were not helped at all and 39% were borderline/unclear. Traces were helpful by mostly showing seizures had stopped. If a trace was not helpful or unclear, it was most commonly due to a lack of documentation.
Conclusion: aEEG is a helpful for neurological monitoring, but further training to improve interpretation and documentation is required. A large prospective study is required to determine who well it can improve PICU care.

Poster 005
Characterizing the features, course and treatment of neuropsychiatric symptoms in children and adolescents with autoimmune encephalitis

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Objective: Early recognition of autoimmune encephalitis (AE) is key, with the prognosis dependent on prompt immunomodulatory treatment. Psychiatric presentations are common in AE and difficult to differentiate from a primary mental health disorder, so the diagnosis is often not considered early. We aimed to describe the psychiatric symptomatology, disease course and management of children with an AE.
Methods: Retrospective review of neuropsychiatric manifestations, course and treatment of children diagnosed with AE between 2016 and 2019 at the liaison psychiatry services in two UK paediatric neuroscience centres. Psychiatric symptoms were categorised in four main clusters (behavioural, speech, mood and psychotic features).
Results: 16 patients (mean age 11.31, SD 2.98; 13 females) were identified of which 7 had NMDAR-antibodies (CSF and/or serum). Two had neurodevelopmental disorders and none of them had previous mental health problems. At presentation, symptoms were only psychiatric in 37.5% (6/16), only neurological in 18.8% (3/16); and mixed in 43.7% (7/16). The most frequent neuropsychiatric symptoms were psychosis (81.2%), disrupted sleep patterns (75%), mood dysregulation (75%), abnormal speech (56.2%), and disordered eating (37.5%). During the course of the illness, all patients had 2 or more psychiatric symptoms, with 43.7% (7/16) presenting concurrent symptoms in four clusters (behavioral, speech, mood and psychotic features), 18.7% (3/16) in three and 37.5% (6/16) in two.
All cases eventually developed neurological symptoms, with delirium (81.2%) and seizures (68.7%) being the most common. Antipsychotics were poorly tolerated and produced worsening of symptoms in 25% of the cases (both NMDAR positive and non-NMDAR patients). Pharmacological treatment with benzodiazepines associated a better response and tolerability.
Conclusion: Within the limitation of this small cohort, we recommend that AE should be strongly considered in children presenting with multiple concurrent psychiatric symptoms, particularly if there had been no prior psychiatric morbidity.

Poster 006
Severity Scoring for Paediatric Autoimmune Encephalitis: PASS

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Objective: The modified Rankin Scale (mRS) is widely used to score disease severity but is coarse (7-point) and insufficiently weighted to non-motor aspects of autoimmune encephalitis (AE). To test the clinimetric properties of the recently developed 30-point Paediatric

AE Severity Score (PASS), we evaluated its discrimination of AE subtypes and relationship with key clinical variables (duration of hospitalisation, long-term outcome) in comparison to mRS.
Methods: Patients admitted to our tertiary centre since 2015 with new onset AE according to consensus diagnostic criteria were included. Weekly PASS and mRS scores were assigned retrospectively by review of electronic patient records over the first 2 months of disease. Statistical analyses utilized Spearman's correlation, Mann-Whitney *U* test and Wilcoxon signed-rank test.
Results: 284 scores were analysed in 23 patients (8 with NMDA-receptor antibody encephalitis [NMDARE]). Median (IQR) PASS was 13 (4–20.5) at peak versus 8 (1–12) at discharge (p=0.01); median mRS was 5 (2.5–5) at peak versus 2 (2–2.5) at discharge (p=0.01). Peak PASS showed stronger correlation with duration of hospitalization compared to mRS (r=0.843 vs 0.707, both p<0.001). Longitudinal PASS plots revealed generally worse severity and longer plateau in NMDARE compared to other AE subtypes, with significant differences at days 0 (12 vs 5, p=0.007), 7 (14 vs 5, p=0.026), 35 (16 vs 7, p=0.004) and 2 months (13 vs 7, p=0.020). Both peak PASS and mRS correlated only weakly with long-term outcome (not statistically significant).
Conclusion: In comparison to mRS, application of PASS in acute AE enabled better delineation of disease severity, which correlated strongly with duration of hospitalization, and revealed significant differences between NMDARE and other AE subtypes. We envisage that PASS could be useful both in clinical trials and to help inform treatment escalation decisions in routine clinical practice.
Acknowledgements:
PASS was developed with our international collaborative group.

Poster 007

A descriptive retrospective single-centre study on clinical profile of acquired central nervous system demyelinating syndromes among a paediatric cohort in Sri Lanka

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Background: Acute demyelinating syndrome (ADS) of central nervous system (CNS) is a spectrum of clinical phenotypes that can overlap and progress to a more severe form over time.
Objective: To describe the initial clinical profiles and subsequent progression with relapses of ADS.
Methods: A single centre descriptive retrospective study. All 35 were less than 17 years 11 months of age when they presented with their first episode of CNS demyelination among a cohort in Lady Ridgeway Hospital, Colombo, Sri Lanka. The data was collected during the last two quarters of 2020 from 2012 to 2020. The validated diagnostic International Paediatric Multiple Sclerosis Study Group (IPMSSG-2012) tool for ADS and pretested interviewer-administered questionnaire were used in the study.
Results: Myelin oligodendrocyte glycoprotein (MOG) associated disease (MOGAD) was the most prevalent ADS and followed by clinically isolated syndrome (CIS) during the first clinical presentation. Acute demyelinating encephalomyelitis (ADEM) is the most common type of presentation among MOGAD, 7/15. Among 20 anti-MOG-antibody negative patients, 14 had CIS, consisting of 9 optic-neuritis (ON) and 5 transverse-myelitis (TM). 10 patients had relapses during the time span. Half of the relapses were MOGAD. 2 had a more relapsing course with 'leukoencephalopathy-like presentation'. Among the relapses, there were 2 cases of paediatric onset multiple sclerosis (POMS). 27/35 fully recovered to the pre-symptomatic base level.
Conclusion: The study reveals that the most common presentation of ADS is ADEM and ON irrespective of anti-MOG antibody prevalence. Alarmingly, the emerging entity of ADS is MOGAD which has a high risk of relapse. However, good recovery is noted in the absence of relapses. Increasingly, anti-MOG antibody seropositive is noted among ADEM. That said, the frequent relapsing nature in the absence of anti-MOG antibody necessitates investigation for POMS. However, more multicenter prospective studies and systematic reviews would give better insight on this ever-evolving ADS disease progression.

Poster 008

'It gets worse, before it gets better'-Outcome in a cohort of children presented with neurological manifestations of dengue fever

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Objective: To analyze the neurological outcome in children admitted with various neurological features of dengue fever following discharge.
Methods: We performed a prospective study in children aged 1 month to 16 years in a tertiary hospital in south India. Children who were admitted with a diagnosis of dengue fever and had neurological manifestations at the time of admission were followed up and neurological examination was performed after 1 year from the time of discharge.
Results: Among 244 children who presented with dengue fever, 9 children had neurological features at the time of admission. All 9 children underwent magnetic resonance imaging (MRI) of which 4 were normal. Clinical neurological deficits along with MRI changes were present in 5 children at the time of discharge. Neurological examination performed in out-patient clinic following 1 year of discharge was normal and did not reveal any focal neurological deficits.
Conclusion: The varied clinical presentation and lesser incidence in children makes neurological manifestations of dengue fever an unexplored area. In spite of having significant MRI changes and clinical neurological deficits, it was interesting to note complete recovery in all children. Larger multi-centric studies in future will help strengthen the evidence.

Poster 009

Isolated paediatric CNS presentations of haemophagocytic lymphohistiocytosis (HLH); a 9 patient case series

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Isolated CNS presentations of haemophagocytic lymphohistiocytosis (HLH), traditionally a systemic inflammatory condition,

have been reported in adults and children. We identified nine patients with a diagnosis of isolated CNS familial HLH (fHLH) with symptom onset <18 years of age, and one asymptomatic sibling. Children with atypical chronic/recurrent CNS inflammation should be considered for immunological and genetic panel testing for fHLH even in the absence of any systemic inflammatory features. Despite haematopoietic stem cell transplantation (HSCT) being a mainstay of treatment, treatment failure and high morbidity and mortality post HSCT suggest that alternative immune therapies may be worth considering.

Poster 010

A case of acute encephalopathy with biphasic seizures and delayed diffusion changes

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Acute encephalopathy with biphasic seizures and delayed diffusion changes (AESD) is an extremely rare syndrome outside Asia. AESD is diagnosed based on clinic-radiological correlation. Influenza or human herpesvirus 6 infection have been most commonly isolated in previously healthy children with AESD and there is possible correlation with genetic abnormalities such as mutations in the SCN1A gene. We report a 2 year old previously fit and well white female who presented febrile status epilepticus at day 3 of an upper respiratory tract infection with subsequent prolonged left facial palsy and left hemiparesis. Brain MRI on day 4 showed swelling and diffusion restriction of the right hippocampus, without any other focal abnormality or signs of ischaemia. On day 6 she presented clusters of focal left sided seizures, non-responding to treatment Levetiracetam and sodium valproate add on. Repeated brain MRI on 7 showed prolonged and diffuse diffusion restriction over the whole right hemisphere, which along with the characteristic clinical presentation led to the diagnosis of AESD. She received high dose IV steroids with taper over 6 weeks starting on day 9. The seizures stopped on day 10 but motor function recovery was slow. CSF analysis showed no signs of infection. Nasopharyngeal swab was positive for Bocavirus and she had positive antibodies for SARS-COV-2 with negative PCR. Genetic investigations were requested and are pending. This case illustrates the importance of repeated brain imaging in abrupt onset refractory seizures with abnormal neurological examination which can lead to early diagnosis and treatment. More studies are needed to investigate the correlation between SARs-COV-2 or Bocavirus and AESD.

Poster 011

A rare case of norovirus encephalitis

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Objective: To describe a case of norovirus encephalitis.
Method: Case report.
Report: A four-year-old male with panhypopituitarism presented with a 6-hour history of vomiting and fever. He developed status epilepticus in the setting of hypoglycemia (glucose 1.6mmol/L) and fever (38.9°C). However, after cessation of seizures (IM glucagon and benzodiazepine), he had a persistently low Glasgow coma scale (GCS), tachycardia and persistent hypoxia. He was intubated and transferred to the PICU. He remained seizure-free and sedating medication weaned. He remained persistently febrile. Norovirus was detected in stools. Brain MRI (day 2 of admission) demonstrated small focal area of restricted diffusion (RD) in the left premotor cortex. Lumbar puncture was negative (WCC 1, gram stain and viral panel). Creatine kinase (peak:2468mmol/L) and c-reactive protein (Peak:129mg/L) remained persistently elevated with transaminitis. He initially improved, he was drowsy but following commands. On day 3 of admission, he had two generalised onset-motor seizures (normal glucose). Following this, GCS remained persistently reduced (9–10), he was fixing and following but was non-verbal with new spasticity and brisk reflexes. Repeat MRI brain (day 6) demonstrated new extensive RD and oedema in both hemispheres (cortical, subcortical and deep white matter), left greater than right. CSF was negative for norovirus. To date, there has been minimal improvement.
Conclusion: The clinical presentation and MRI findings are in keeping with norovirus encephalitis presenting with biphasic seizures and late RD on MRI. Norovirus is a common cause of gastroenteritis, usually presenting as a self-limiting illness of vomiting, diarrhoea and fevers. Encephalitis is a rare complication, and CSF can be negative, like in our case. The outcome is poor, especially when associated with early neurological symptoms and elevated serum creatinine. Norovirus encephalitis is an important differential to consider in a patient presenting with seizures and reduced GCS in the setting of norovirus.

Poster 012

Cerebral fat embolism in the absence of intracardiac shunting

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Introduction: Cerebral fat embolism (CFE) is a rare phenomenon in paediatric settings and is usually seen post-trauma in patients with pre-existing intracardiac shunting. We present a rare case of CFE in the absence of cardiac anomaly.
Case: A 16 year old previously fit and well male sustained open fractures of the right lower limb following a fall from a motorcycle without reported head injury. His GCS was 15 at presentation. He underwent internal and external fixation of his multiple fractures. Post-operatively, he developed altered sensorium and abnormal posturing without respiratory compromise and did not require oxygen at any stage. He consequently had an urgent replacement of the external fixation with an MRI compatible intramedullary nail to facilitate imaging. MRI brain showed bilateral diffuse T2/FLAIR white and deep grey matter hyperintensities with diffusion restriction. These appearances were highly suggestive of cerebral fat embolism (CFE). Paradoxical embolism was excluded following a normal cardiac echocardiogram. Despite the extensive changes noted on brain imaging, he had an excellent recovery over a few weeks. On discharge, he was independently mobile with no neurological

deficits and had no speech, swallowing or other significant difficulties.
Discussion: This case supports a rare, previously described mechanism, where fat microglobules may sometimes be too small and malleable to cause pulmonary injury, and can be filtered through the lung capillaries into the arterial circulation. Our case supports this theory as the patient had no evidence of hypoxia at any stage and only had cerebral complications of fat embolism from a long bone fracture.
Conclusion: CFE should be considered in all patients with long bone or pelvic fractures who develop sudden onset neurological symptoms and more importantly, can occur in the absence of intracardiac shunting or pulmonary symptoms.

Poster 013

Petrous apicitis causing a unilateral sixth nerve palsy in a 4-year-old

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Objective: To report a case of sixth nerve palsy due to petrous apicitis secondary to acute otitis media and to discuss the mechanisms behind this presentation
Case: A 4-year-old was referred to neurology with a new onset squint and found to have right sixth nerve palsy. Two weeks prior, he was seen by GP for right sided otalgia, headache and commenced on oral antibiotics. He was systemically well on presentation to us without any earache, fever or vomiting. There was no involvement of trigeminal nerve and pupillary reactions were normal. MRI brain without contrast failed to reveal any abnormality, but when a contrast study was done a few days later, it showed enhancing lesion in the right petrous apex with thickening of lining of right internal auditory canal. He was given a 2 week course of IV Ceftriaxone and Metronidazole and further 6 weeks of oral antibiotics. He is being followed up by the ENT surgeons.
Discussion: Petrous apicitis is a known complication of acute otitis media, as acute otitis media can extend medially into a pneumatized petrous apex. The classic triad known as Gradenigo syndrome includes abducens nerve palsy, symptoms of otitis media, and retro-orbital pain in the distribution of the trigeminal nerve. More commonly cranial nerve palsies can be the presenting features. The entrapment of the abducens nerve under the petrosphenoid ligament of Gruber as it runs within the Dorello's canal manifests as lateral rectus palsy.
Conclusion: It is essential to have a high index of suspicion even when the child is not acutely ill and a contrast MRI scan is recommended in the presence of history of acute otitis media.

Poster 014

An emerging infectious cause of flaccid paraparesis/quadriparesis

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A previously healthy 7 year old male developed fever for 2 days, followed by lower limbs weakness that rapidly progressed to upper limbs and bulbar muscles. He subsequently developed increased work of breathing followed by a rapid deterioration in his respiratory effort and was intubated and ventilated for respiratory failure. There was no history of travel, or head and spinal injury and was fully immunized. Physical examination showed quadriparesis, truncal and limbs hypotonia, areflexia with no sensory level and excessive drooling. CSF examination showed normal protein, 17 WBC, culture and viral PCR were negative. Stool PCR was positive for enterovirus. CT and MRI head were normal. MRI spine showed subtle T2 high signal affecting the central cord affecting the cervical and lower thoracic cord extending to the conus, without nerve root enhancement. Nerve conduction studies/electromyography showed patchy affection of lower motor neurons or to motor axons in acute stage of evolution. Enterovirus 68 was confirmed on respiratory PCR and in view of clinical, radiological and microbiological evidence, a diagnosis of Enterovirus 68 related acute flaccid myelitis was made. He received presumptive treatment with antibiotics and acyclovir initially, then courses of intravenous immunoglobulin (IVIG) and steroids. He received tracheostomy, nasogastric tube feeding and long- term neuro-rehabilitation.
Discussion: Acute flaccid myelitis (AFM) is an uncommon but serious neurological condition that tends to occur in outbreaks every few years. More than 90% of patients with AFM had a mild respiratory symptoms or fever consistent with a viral infection before they developed AFM. Viruses confirmed to cause AFM include; coxsackievirus A16, Enterovirus-A71, and Enterovirus-D68. Acute flaccid myelitis is an important differential to consider in acute flaccid paraparesis/quadriparesis in addition to the common possibilities of GBS and acute transverse myelitis. Being aware of EV-68 related AFM is important from a public health perspective as there have been outbreaks of EV-68/EV-71 in many geographical areas.

Poster 015

Invasive pneumococcal disease caused by non-vaccine serotype: a case report

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Objective: Streptococcus pneumoniae is a major cause of meningitis in young children and associated with significant neurologic and long-term sequalae. The introduction of multivalent conjugate pneumococcal vaccines has led to a decline in invasive pneumococcal disease caused by serotypes included within the vaccine. Here, we report a case of pneumococcal meningitis caused by a serotype not covered by the vaccine, suggesting serotype replacement.
Case: Case of a 3-month-old female presenting with a 1-day history of fever and reduced feeds. She was born prematurely at 36 weeks gestation without complication; she had received the first 3 sets of immunizations as per schedule, being fully vaccinated for her age. Examination revealed her to be febrile, irritable, with a soft fontanelle, with mottled peripheries and with no neurological deficit. A full septic screen was conducted and broad-spectrum antibiotics commenced. Fever lasted for 4 days and on day 6, she had a focal left sided seizure, which bilaterally generalized. Seizure duration was approximately 60 minutes and aborted following 2 doses of benzodiazepine and a loading dose of Levetiracetam. She had intravenous antibiotics for 6 weeks, there were no further seizures and is maintained on Levetiracetam.
Results: CSF microscopy revealed an elevated white cell count with primarily polymorphonuclear leukocytes. Within 36 hours,

streptococcus pneumoniae was isolated from both cerebrospinal fluid and blood samples. MRI brain post seizure revealed abnormal CSF signal and leptomeningeal enhancement consistent with meningitis, a small cortical vein thrombosis overlying the right frontal lobe and small empyema overlying the right hemisphere. A repeat scan 5 weeks later revealed no evidence of empyema or cortical vein thrombosis.
Conclusion: Invasive pneumococcal disease caused by non-vaccine serotypes continues to present a challenge and highlights the need for serotype replacement and new treatment strategies.

Poster 016

Acute encephalopathy with biphasic seizures and late diffusion restriction: characteristic MRI brain findings

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A 15-month-old, pre-morbidly normal female presented with atypical febrile seizure with low GCS. She had a biphasic clinical course with relapse of seizures following around 10 days of seizure control. She subsequently developed acute encephalopathy with loss of previously acquired milestones, lack of visual interaction, loss of response to auditory stimuli and profound truncal weakness. Respiratory PCR was positive for adenovirus while blood PCR was positive for adenovirus and EBV. CSF analysis was unremarkable. MRI head showed diffuse symmetric areas of restricted diffusion in bilateral cerebral hemispheres involving subcortical white matter mainly within parietal and temporal lobes and within anterior and lateral aspects of bilateral thalami. These areas of restricted diffusion demonstrated high T2/FLAIR signal. These typical MRI findings in conjunction with the classic clinical course was suggestive of acute encephalopathy with biphasic seizures and late diffusion restriction (AESD). She received treatment with intravenous steroids, intravenous immunoglobulin and intense neurorehabilitation following which there is an ongoing improvement in her neurological function. Acute encephalopathy with biphasic seizures and late diffusion restriction (AESD) is an acute encephalopathy syndrome diagnosed by characteristic clinicoradiological findings. A biphasic clinical course is typical which is heralded by a prolonged febrile seizure followed by improved consciousness. 3 to 7 days after onset, a cluster of seizures along with encephalopathy becomes apparent. The typical finding on MR imaging from 3 to 9 days after onset is widespread reduced diffusion. Depending on the distribution of brain lesions, there are two sub-groups, with or without central grey nuclei involvement, with the former having worse outcomes. Affected children display various levels of neurological sequelae. There is no consensus on treatment regimen. There is anecdotal evidence for use of steroids/intravenous immunoglobulins believing it is a post-infectious inflammatory syndrome. Timely diagnosis of this condition is important for prognostication.

Poster 017

A case of CNS-isolated haemophagocytic lymphohistiocytosis (HLH)

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Isolated CNS haemophagocytic lymphohistiocytosis is a rare neuroinflammation without the laboratory finding of HLH disease. It has clinical and radiological characteristics however there is an overlap with other neuro-inflammatory disorders. We report an 18 year old male who presented at the age of 4.5 years with right hemiplegia. He was investigated and thought initially to have a stroke or brain tumour. Following investigation, he was treated for acute demyelinating encephalomyelitis (ADEM) although he had no encephalopathy and had 3 days of IV steroids which improved his right sided weakness with residual impairment. He had a second episode when he was 17-years-old presenting with ataxia and dysarthria which responded to IV steroid with improved imaging however he had further deterioration with dysarthria and slurred speech. His MRI was reviewed and he was diagnosed with CNS-isolated HLH and needed bone marrow transplant. This illustrates the difficulty of diagnosing CNS-isolated HLH and the need to consider it in the differential diagnosis with children with refractory or recurrent neuroinflammation without clear etiology to prompt early treatment.

Poster 018

Recurrent herpes simplex virus-1 encephalitis in a young child

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Introduction: Herpes simplex virus (HSV) is the most common cause of viral encephalitis with an incidence of 1 in 100 000 to 150 000. Although a treatable condition, it is associated with high morbidity (60%) and mortality (20%). Recurrent HSV encephalitis (HSE) is rare. Toll like receptor 3 (TLR3), interferon α/β, Janus Kinase (JAK) and STAT1/2 are all implicated in the antiviral neuroimmune response. Abnormalities in these pathways, may confer increased risk for recurrent HSE.
Case Report: A 2.5 year old male presented with a history of vomiting, fever and headache. He was previously treated for fulminant HSV1 aged 7 days, with positive CSF HSV-1 PCR. He remained developmentally typical following his initial hospitalization. He presented with recurrent mild cutaneous HSV throughout infancy (never accompanied by clinical or CSF confirmed HSE). Immune function work up was normal. Two next generation sequencing panels were undertaken (TIGR panel, GOSH, London and Invitae immunodeficiency panel, San Francisco), neither of which revealed a known pathogenic mutation associated with recurrent HSV. A VUS in STAT1 was found on the TIGR panel, but the patient had none of the phenotypic features associated with STAT1-associated immunodeficiency and functional studies subsequently demonstrated no evidence of either gain- or loss-of-function in STAT1. Following a year free of cutaneous HSV recurrence, the patient's acyclovir prophylaxis was discontinued. He presented 3 weeks following discontinuation. HSV1 was

isolated on CSF PCR. MRI brain showed T2 hyper-intense cortical and subcortical signal involving the medial temporal lobe and insular cortex on the left side in keeping with HSE. EEG showed excess diffuse slow wave activity with left sided predominance. He was treated with 21 days IV acyclovir and transitioned back to oral aciclovir prophylaxis following negative HSV -1 CSF PCR. He remains seizure free and developmentally typical. Whole exome sequencing is currently being undertaken to screen for a genetic basis for his recurrent disease.
Conclusion: Relapse of HSE is reported in 12% of cases, and can occur even when no obvious pathogenic mutations are found in genes known to be associated with recurrent HSV. Early diagnosis and treatment is critical to limit adverse neurodevelopmental sequelae.

Poster 019

An unusual case presentation of GBS overlapped with transverse myelitis in an adolescent female

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Introduction: A teenager presented with Guillain-Barre syndrome (GBS) overlapped with transverse myelitis (TM).
Material: 13-year old female presented with weakness and paraesthesia in lower limbs and loss of bladder and bowel sensation, progressing over 2 days. She reported a fall on a trampoline a day before the symptoms onset. She had received the first HPV vaccine dose 2 weeks before. She had hypotonia with power 0/5 MRC in both lower limbs, absent deep tendon reflexes in lower limbs, loss of sensation below T12 level and loss of abdominal reflexes. She had bladder and bowel dysfunction. Differentials TM, GBS, non-polio like illness, traumatic neuropathy were considered.
Methods: FBC, biochemistry, inflammatory markers and VEP were normal. CSF showed albuminocytologic dissociation with protein 787mg/L, negative neurotropic virus panel and negative oligoclonal bands. Coronavirus PCR was negative. Serum Anti MOG and Aquaporin 4 were negative. Nerve conduction study demonstrated bilateral multiple level severe axonal nerve root lesions. She had three spinal MRIs, showing T2 signal change at the conus extending up to T9/10 with abnormal enhancement of the cauda equine nerve roots.
Result: She received high pulse steroids with taper over 6 weeks, IVIG twice, double filtration plasmapheresis and total plasma exchange with minimal improvement clinically.
Discussion: Differentiating between GBS and TM may be clinically challenging. However, repeated imaging, nerve conduction studies, and CSF examination can lead to a diagnosis.
Conclusion: The patient's clinical presentation, imaging and neurophysiological findings were suggestive of GBS overlapped with TM of unclear aetiology. Previous HPV vaccine may be related. Despite multiple immunomodulatory treatments she showed minimal improvement. Chronic immunosuppression was not suggested due to current lack of evidence of benefit overcoming the risks. A precise diagnosis may be facilitated by repeated neuroimaging and neurophysiological investigations.

Poster 020

Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS)

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Background: Mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinicoradiological syndrome characterized by transient mild encephalopathy and magnetic resonance imaging (MRI) findings of a reversible lesion in the splenium of the corpus callosum. It can be related to infectious and non-infectious conditions. Patients with MERS generally present with central nervous system symptoms such as disturbance of consciousness, headache, and seizure. Most patients have mild clinical course. All patients recover with supportive treatment within a month, most of them within a week.
Case description: We describe the case of a 4 year old female who presented to A&E with 4 days history of fever, headache, vomiting and increased sleepiness. Her throat was inflamed. WCC and neutrophils were mildly raised. CRP was 57mg/L. MRI showed a focal lesion of restricted diffusion in the splenium of corpus callosum. The rest of her brain looked normal. Viral PCR on throat swab was positive for adenovirus. CSF was sterile with normal biochemistry and microscopy. Its viral PCR was negative. Blood culture did not show any growth. The female recovered spontaneously with supportive treatment in 1 week and was discharged home.
Conclusion: MERS, although uncommon, is well described in literature as an acute and self-limiting disease with excellent prognosis. MRI lesions are usually quite typical and disappear completely in all patients within couple of months. It is important for paediatricians to be aware of this condition to avoid unnecessary investigations and reassure parents.

Poster 021

Cerebral fat embolism syndrome (FES) following sickle cell crisis: Case report

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Objective: To highlight hitherto under-recognised cerebral fat embolism as a cause of stroke in patients with bone crises in homozygous sickle cell anaemia.
Methods: Illustrative case report and review of literature.
Introduction: Painful bone crises resulting in bone marrow necrosis is well recognised in patients with homozygous sickle cell anaemia (HbSS). It can lead to dissemination of fat emboli and fat embolism syndrome (FES) including stroke in a minority of HbSS sufferers. This is under-recognized.
Results: A female teenager with homozygous HbSS presented with pyrexia, hip pain, thrombocytopenia and deranged inflammatory markers. She was diagnosed with 'painful sickle crisis' and given supportive care including hydration, antibiotics, patient-controlled analgesia (PCA). Admission GCS was 15/15. A day later, she became confused and drowsy (GCS 9/15) without lateralising

signs. This did not improve with stopping PCA and naloxone. Urgent CT brain showed dilated right temporal horn of lateral ventricle with cerebral oedema. She was intubated and transferred to paediatric intensive care unit. MRI brain revealed bilateral multiple micro infarcts in both cerebral hemispheres and 'starfield' pattern and haemorrhages consistent with cerebral fat embolism. She underwent daily plasma-red cell exchanges. Cardiac echo showed patent foramen ovale with left to right shunting. Her GCS normalised after 3 days. The full impact of this cerebrovascular occlusive event is to be assessed as she receives intensive rehabilitation inputs.

Conclusions: Cerebral fat embolism syndrome is a devastating albeit rare complication of homozygous sickle cell disease. Clinical features include fever, painful extremities, chest pain, increased work of breathing, reduced conscious level and thrombocytopenia in common with other sickle emergency presentations. Prompt recognition and urgent daily plasma-red cell exchange are associated with improved outcomes. Paediatricians who regularly treat children with sickle cell disease should be aware of this hitherto under-recognised CNS complication to ensure optimal management and outcomes.

Poster 022

Reversible splenial lesion syndrome associated with idiopathic intracranial hypertension

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Reversible splenial lesion syndrome (RESLES) is a rare clinico-radiological condition encompassing isolated lesions of the corpus callosum and myriad aetiologies and neurological symptoms. We present an unusual case of a child presenting with RESLES associated with idiopathic intracranial hypertension (IIH) as well as the absence of encephalopathy, seizure or motor deterioration. A 9 year old male patient, with no past medical history of note, presenting reporting headaches and vomiting. Over the next few days he developed a sixth cranial nerve palsy. On examination he was noted to have horizontal diplopia, visual field deficit and bilateral papilloedema, confirmed on B-scan ultrasonography. CT brain did not show any abnormality. MRI including venogram and diffusion weighted imaging (DWI) was felt to show a lesion of the splenium of the corpus callosum and reduced diffusion in keeping with RESLES. Lumbar puncture revealed a raised cerebrospinal fluid pressure of over 40 mmHg, and was reduced accordingly with initial improvement of clinical symptoms. The patient required multiple procedures and the commencement of Acetazolamide to achieve resolution of clinical symptoms. Cerebrospinal fluid was otherwise unremarkable, including negative cultures, viral PCR, Lyme serology and MOG and NMDA antibodies. Repeat MRI the following month demonstrated resolution of the lesion with no other abnormality of note. Although the clinical symptoms and radiological features are often reversible, there is little literature on RESLES and its associations and prognosis, and this is mainly focused on adult populations. The case demonstrates the importance of radio-clinical correlation both in reporting but also requesting, as the diagnosis of RESLES can be complex and dependent on DWI. Further work may be needed to evaluate the prevalence of the association with IIH and relative prognosis.

Poster 023

Novel observation of haemorrhagic stroke as a manifestation of severe hypertriglyceridaemia in type 1 Diabetes with DKA

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Objective: To highlight haemorrhagic stroke as a novel presentation of hypertriglyceridaemia in context of new onset type 1 Diabetes with DKA.

Methods: Case report and literature review.

Introduction: A 11-year old male with autism and ADHD on methylphenidate presented with new onset type 1 Diabetes Mellitus in severe DKA (pH 6.9, Base deficit –24.7, HCO3 3.1, ketones 4.5), AKI and low GCS. Urgent CT head showed a haemorrhagic mass lesion with blood products of different ages and signal intensity, in right frontal lobe, extending to the basal ganglia, with MRI confirming these to be haemorrhagic. CT angiogram and venogram was normal, and carotid dopplers demonstrated increased right sided flow velocity consistent with likely vasospasm. Plasma triglycerides were significantly elevated at >77 (normal 0.5–2mmo/l). He was intubated, ventilated and transferred to PICU where he had intracranial pressure monitoring and multi-organ support. He was densely hemiplegic on his left side. His DKA and hyperlipidaemia resolved with insulin therapy and fluids on day 4. Intracranial lesions were managed conservatively. His methylphenidate was replaced with clonidine, improving his appetite and with more balanced nutritional intake.

Conclusions: Severe hypertriglyceridaemia (triglycerides >22.6 mmol/l) is a known but very rare complication of diabetes with a prevalence of 8% in adults with DKA but with little data in children. The exact mechanism is unclear but transient insulin deficiency may decrease the activity of lipoprotein lipase, coupled with gene abnormalities in the enzyme. It contributes to cerebral oedema in DKA by increasing plasma viscosity and reducing cerebral blood flow causing ischaemia and oedema. There has been no documented cases in the literature of haemorrhagic stroke as a consequence of severe hypertriglyceridaemia in children. This report highlights this novel, hitherto unknown complication where the mechanism is presumably also due to cerebral vasospasm from extreme hyperviscosity.

Poster 024

'Two feet but too many shoes' – a prospective case series of children presenting with acute hemiplegia

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Objective: To highlight the common presentations of uncommon causes of acute onset hemiplegia in children.

Methods: We performed a prospective study in children aged 1 month to 16 years who presented with acute onset hemiplegia to children's emergency in a tertiary hospital in south India for 1 year. The various presentations are as follows:

Case series: (A) 3-year-old female with right sided headache and left shoulder pain which evolved into left hemiparesis. Imaging

showed hyper-intense C5–C6 and posterior cord from C7–C11. She showed dramatic improvement with IV methyl-prednisolone.
(B) 6-year-old female with brief headache followed by right dense hemiplegia. Waxing and waning course of the weakness multiple times the last few days. MRI showed right sided small acute ganglio-capsular infarcts. Prothrombotic work-up was positive for factor V Leiden mutation.
(C) 3-year-old female with acute right sided hemiparesis following 2 days fever. Previous similar episode 2 months back resolved spontaneously. Imaging showed left ganglio-capsular infarct and 90% stenosis of the distal M1 MCA.
Discussion: Although infections were found to be the most common cause for children with acute onset hemiplegia in developing countries, our children were found to have some of the more uncommon diagnoses. Child A had demyelination confined only to the cervical cord which is an uncommon cause of childhood stroke. Child B with factor V mutation, which again is an uncommon cause of intermittent hemiplegia. Although child C had stenosis of right MCA, we could not attribute an underlying pathology.
Conclusion: The age or the clinical presentation or the predisposing conditions do not reveal the actual etiology of hemiparesis. However, early recognition and a structured evaluation will help in diagnosis and management. Establishment of a care pathway in resource limited settings will help unveil many rare conditions.

Poster 025

A curious case of probable subacute sclerosing panencephalitis in a fully vaccinated 8-year-old female responsive to ribavirin and interferon with absent previous measles infection

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Background: Subacute sclerosing panencephalitis (SSPE) is a destructive cerebral disease due to measles virus, usually following a latent period of 7 to 10 years after an infection. Measles vaccination in Sri Lanka during childhood has made this an almost non-existent neurological sequela. But rare cases of SSPE have been reported, in the subcontinent, in fully vaccinated children, without a history of measles.
Case history: This is a case of an 8-year-old female vaccinated with live measles vaccine at the age of 9 months and at 3 years (in accordance with the national immunization schedule in Sri Lanka), without a history of measles, admitted as an emergency, with complex partial seizures on the left side rapidly progressing to an encephalopathy leading to intubation and ventilation. She had a 1-month history of behavioral change, and a week prior to admission had myoclonic jerks on the left side upper limb. EEG showed periodic complexes which were characteristic of Rademaker complexes and MRI showed peri ventricular changes. MRS revealed choline/creatinine ratio reduction. Blood and CSF showed high measles IgG above 5000 IU/l. After starting ribavirin and intrathecal interferon alpha with the ketogenic diet, she was seizure free and extubated after 1 week.
Discussion: Our child had been fully vaccinated and did not have a history of measles. Asymptomatic infection before vaccination in the past cannot be ruled out and may explain why she developed SSPE as it is not reported with the vaccine. History was brief but classic stages described were identified. Diagnosis of SSPE was suspected on the EEG changes thus its importance with rapidly progressive encephalopathy. Without initiation of Ribavirin and interferon, this would have been fatal, with the use of ketogenic diet, 3 months later she was stable, responsive to mother, and absent of myoclonic jerks.

Poster 026

Risk of COVID-19 in children treated for demyelinating disorders in the UK

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Objective: Paediatric neurologists are concerned about the risk of COVID-19 in children with demyelinating disorders receiving immunomodulatory treatment. To investigate this, we collected data via the UK Childhood Neuro-Inflammatory Disorders (UK-CNID) network of the British Paediatric Neurology Association (BPNA).
Methods: Survey of paediatric neurologists managing unvaccinated UK children (<18 years) with a demyelinating disorder (multiple sclerosis [MS]; neuromyelitis optica spectrum disorder [NMOSD] and myelin oligodendrocyte glycoprotein antibody disease [MOGAD]) on immunomodulatory therapy with SARS-CoV-2 infection confirmed by reverse transcriptase–polymerase chain reaction (RT-PCR) of nasopharyngeal swabs between March and December 2020.
Results: Of 151 UK children (MS 98, MOGAD 37, NMOSD 16) with a median age of 9 years (range 6–18y), with a demyelinating disorder, nine (6.0%) had a positive PCR for SARS-CoV-2. Five had MS and four MOGAD. Four were from south Asian or south-east Asian, four were White and one was mixed White and south Asian. Seven children had COVID-19 symptoms; two were asymptomatic. Two required a brief hospital admission for typical COVID-19 respiratory symptoms and the remaining five had mild symptoms including fever, rash, cough and headache. One with MOGAD, treated with azathioprine, developed transverse myelitis 12 days after COVID-19 onset. She recovered fully with a course of corticosteroids. MS patients were on following disease modifying therapies; dimethylfumarate (n=2), fingolimod (n=1); natalizumab (n=1) and ocrelizumab (n=1). MOGAD cases were on the following immune therapy: combination of oral prednisolone and intravenous immunoglobulin (n=2), prednisolone steroids (n=1) and azathioprine (n=1).
Conclusions: In contrast to adult patients, who often have underlying co-morbidities and advanced neurological disabilities, we have identified that children treated for demyelinating disorders appear to have a milder COVID-19 course. Whilst the number of children treated for demyelinating disorders that developed COVID-19 is low, the overall mild course described may provide reassurance to neurologists, patients and family members.

Poster 027

Neurological and radiological findings associated with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in children

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Background: Neurological manifestations have been reported both in adults and children with coronavirus disease 2019 (COVID-19). Paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) is a recently described severe post-infectious immune-mediated disorder.
Objective: Our aim was to report neurological manifestations of children with PIMS-TS.
Methods: Patients (<18y) presenting to Great Ormond Street Hospital between April 4, 2020, and May 1, 2021 fulfilling PIMS-TS criteria, were included. Clinical and paraclinical features were retrieved retrospectively from electronic patient records.
Results: Data was available for 125 patients who presented during the study period. Median age was 10 years (IQR 7, 12), 71 (56.8%) were male and 96 (76.8%) were of non-white ethnicities. New-onset neurological symptoms were reported in 73/125 (58.4%); headaches (n=47), encephalopathy (n=41), hallucinations (n=15), ataxia (n=12), dysarthria/dysphonia (n=12), peripheral nerve involvement (n=3), and seizures (n=1). Thirteen patients had CSF examined; one patient had 118 leukocytes in CSF. Abnormalities were noted in 16/32 patients with neuroimaging, with splenium of the corpus callosum signal changes most commonly seen in 9 patients. An excess of slow activity was found in 78/98 who had an EEG; 38 mild, 34 moderate and 7 had severe encephalopathy on EEG. Myopathic and neuropathic changes were seen in 7/12 who underwent nerve conduction studies and electromyography (EMG). Children with neurological involvement had higher peak inflammatory markers and were more likely to be ventilated and require inotropic support in PICU ($p<0.05$).
Conclusions: Children with PIMS-TS presented with new neurological symptoms involving both the central and peripheral nervous systems, in the absence of respiratory symptoms. Neurological symptoms were seen more frequently in more severe presentations.

Poster 028

Impact of lockdown for COVID-19 on care-givers of children with neurological diseases in Enugu, Nigeria

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Objectives: To understand the impact (health, cognitive, economic, and psychological) of the COVID-19 lockdown on children with chronic neurological disorders (epilepsy, cerebral palsy, autism, ADHD) in Nigeria.
Methods: A focused group discussion of caregivers and children with chronic neurological conditions (epilepsy, cerebral palsy, brain tumor and muscular dystrophy) was conducted. Nine caregiver-patient pairs participated in the discussion while observing all precautionary measures. The responses of the participants were recorded, transcribed and analysed.
Results: There was limited access to consulting physicians in the hospital to review the child's health status, and lack of money to purchase drugs as parents' means of livelihood were disrupted. Findings indicated that children seemed to have forgotten what they learnt in the previous academic period. Some of the children have torn their books, given that learning tutors gave out the books for children to practice at home. The lockdown policy imposed hunger in the households as parents couldn't attend to their various jobs. Households rarely eat recommended daily servings and mix of food. Some of the caregivers lost their jobs, others had their shops and businesses locked down, leading to inability to contribute money for household feeding. Children had access to cloth face masks. However, children seldom adhere to the use of facemask when necessary. Regular hand washing was common. Only one participant reported availability and use of hand sanitizer. The lockdown of worship centers conferred a sense of anger, frustration, and hopelessness among some of the participants. Caregivers believed they lost social interactions including drinking with friends.
Conclusion: The COVID-19 lockdown had untoward effects on different aspects of the lives of children with chronic neurologic illnesses requiring the development of well adapted local strategies to mitigate unintended effects on children.

Poster 029

Home schooling and lock-down can foot the blame for an interesting COVID-19 complication

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Objective: The period of enforced school-closures from March 2020 to March 2021 has taken a huge toll on children in Ireland. Ill-effects of COVID-19 including direct infection, social isolation and mental health problems are clear to see. However, not all complications are so obvious. We examined the findings of paediatric nerve conduction studies (NCS) carried out at a tertiary general hospital in the South of Ireland. We aimed to highlight at increase in the incidence of 'idiopathic' common peroneal nerve palsies arising during the COVID-19 social and school restrictions.

Methods: We examined the results from all NCS performed on children (<18 years) during the two and a half year period between January 2019 and July 2021. We correlated our findings with the clinical patient information from the time of the neurophysiological investigation.
Results: One hundred and two NCS examinations were performed on 95 different children between January 2019 and July 2021. During the 1-year period before the COVID-19 pandemic arrived in Ireland (January 2019 to January 2020) there was only a single case of paediatric common peroneal nerve palsy recorded. This case had an obvious precipitant cause (recent significant weight loss). During the time of school closures, there were five cases including one case of bilateral common peroneal nerve palsy. MRI and examination identified no cause, and all children reported adopting abnormal sitting postures while carrying out schoolwork at home (prolonged kneeling, side sitting, unsuitable seating).
Conclusions: Children have been seen as invisible victims of the COVID-19 pandemic, and although the direct health burden of COVID-19 infection on children is lower than in vulnerable adults; there are many negative social, educational, psychiatric and indeed neurological effectors of paediatric health arising from the COVID-19 crisis. We hypothesise that the prolonged school closures led to an increase in 'idiopathic' paediatric common peroneal nerve palsies, which are otherwise extremely rare in this population.

Poster 030
Unusual neurological manifestations in children during the COVID-19 pandemic

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Objective: To present paediatric cases of unusual neuroinflammatory conditions encountered during the COVID-19 pandemic in Trinidad & Tobago.
Methods: Retrospective study design. Inpatient paediatric patients (aged 0–16 years) hospitalized for neurological complaints from June 2020 – August 2021 at EWMSC. Outcome measures were age at presentation, sex, ethnicity, diagnosis, radiological findings, blood/CSF findings, COVID-19 PCR and antibodies testing, treatment, outcomes and other systems involved.
Results: Twenty (20) patients (aged 4-months-old to 15-years-old) had documented neurological involvement. 50% had a diagnosis of ADEM/ADS/AHNE; 45% had a diagnosis of either CNS vasculitis (n=3), autoimmune encephalitis (n=3) or GBS (n=3); 5% had a diagnosis of acute COVID-19 encephalitis. 70% were of African descent. The youngest age group (0–4 years) (n=11) constituted more males (82%) whereas the eldest age group (10–15 years) (n=3) were all females. Neuroimaging findings were corpus callosal lesions; deep white matter T2 hyperintensities; cerebellar involvement; area postrema and brainstem/C-spine involvement; microhaemorrhages and necrotizing/haemorrhagic lesions (peripheral/central). 70% of patients were either SARS-CoV-2 PCR or COVID-19 antibodies positive. Other systems were involved in 40% to 62.5% (n=5) had cardiac involvement (myocarditis, coronary arteries dilatation, valve regurgitation) and 37.5% (n=3) had pancreatic involvement (autoimmune pancreatitis, type 1 diabetes mellitus). Treatment modalities for CNS manifestations (n=17) were clinically based – 24% (n=4) 3rd line treatment, 29% (n=5) 2nd line treatment, 41% (n=7) 1st line treatment and 6% (n=1) requiring no treatment. All 3 patients with a diagnosis of GBS responded appropriately to IVIG. Developmental outcomes were worst in patients with a diagnosis of autoimmune encephalitis.
Conclusion: We have had an explosion of neuro-inflammatory cases since the COVID-19 pandemic began. The range of neuroradiological diagnoses and other systemic involvement (including criteria for PIMS) are interesting, alluding to a neuroinflammatory mechanism. Effects on long-term sequelae and developmental outcomes are concerning in some cases, however, still unknown at this stage.

Poster 031
PIMS-TS: Neurological, quality of life and adaptive functioning outcomes and associated factors

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Background: Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS) causes prolonged hospitalisation and morbidity. The longer term neurological and health outcomes in children following PIMS-TS are largely unknown.
Methods: In this single-institution study, we evaluated the domains of daily living, physical, emotional, and quality of life outcomes at 6 months following PIMS-TS. Data were collected by telephone questionnaire interviews with parents and children and also using standardized assessment tools –PedsQL-Multidimensional Fatigue Scale, and Paediatric Symptom Checklist (PSC).
Results: Data were obtained from 81 children admitted with PIMS-TS between April and August 2020. 49 were males (60%) and 52 (63%) non-white. Median age was 9 years (8–17 years) with length of stay of 6 days (range 1–22 days). Prior to discharge, 34 children (42%) had difficulties with activities of daily living whereas only 5 (6%) persisted on 6 months follow up. Exercise intolerance/mobility difficulty was observed in 40 children (9%) at discharge compared to 20 (25%) 6 months later. Predictors associated with difficulty in exercise tolerance/mobility were obesity (OR=4.0; 95% CI: 1.1–13.7; p=0.03) and older age (OR=1.1; 95% CI: 0.99–1.3; p=0.086). Inflammatory markers on admission (CRP, fibrinogen, D-dimer and ferritin) did not correlate with worse outcome at follow-up nor did sex and length of stay. The PedsQL-Multidimensional Fatigue Scale revealed a median score of 94 (IQR: 83–100) indicating an overall average range quality of life.
The PSC were in line with population prevalence of behavioural/emotional difficulties: 10% had difficulties with attention; 7% and 4% of patients had internalizing and externalizing difficulties, respectively

Conclusion: Overall, patients with PIMS-TS have good short-term outcomes at 6 months with respect to daily functioning, quality of life, and behaviour. One in four had some difficulty with mobility/pain requiring rehabilitation, with main risk factors being obesity and older age. Further studies are required to evaluate long-term sequelae.

Poster 032

[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.]

Two acutely presenting toddlers

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Poster 033

Multiple ischaemic strokes and vertebral artery dissection in a single patient in the setting of asymptomatic SARS-CoV-2 infection

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Objective: To report a 6 year old male who presented with recurrent cerebral infarctions and vertebral artery dissection in the setting of SARS-CoV-2 infection.
Method: Case report.
Results: A previously well 6 year old male presented with a 2 week history of headache, neck pain and ataxia. SARS-CoV-2 was detected on surveillance nasopharyngeal PCR. Neuroimaging revealed a right inferior parietal cortical infarct with absence of flow in the distal right posterior cerebral artery. CT angiography showed no evidence of vertebral artery dissection or cerebral vasculopathy. He was anti-coagulated initially, and post investigations, discharged home on anti-platelet therapy.
He represented 4 weeks later with symptom recurrence. MRI brain on admission displayed a left thalamic infarct. Cerebral angiography showed right vertebral artery dissection with new distal thrombus and bilateral cerebellar infarcts. He was treated with 6 months of LMWH and then changed to antiplatelet therapy. He has had no further events. Thrombophilia, autoimmune and metabolic investigations have been negative. The patient has made a great recovery with minimal circumduction on walking and mild intention tremor.
Conclusions: The risk of stroke in young people has been highlighted in the setting of SARS-CoV-2 infection. The reported incidence of cerebrovascular disease in patients testing positive for SARS-CoV-2 ranges from 1% to 6% in the adult population. In the paediatric population, stroke has been reported in children with PIMS-TS also. The proposed mechanism for such events is a hypercoagulable state caused by viral endothelitis, a post infectious immune mediated response or systemic inflammation. Here, we present an unusual case of multiple remote ischaemic strokes in a child who had concurrent asymptomatic SARS-CoV-2 infection without evidence of further organ dysfunction or acute inflammation.

Poster 034

A mixed methods study to develop a core outcome set for refractory childhood epilepsy treated with ketogenic diet therapy (CORE-KDT): Preliminary findings

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Objective: Clinical trials contain a wide range of outcomes with differing methods of measurement and reporting. However, these are often not the most important perceived by patients and decision makers. A core outcome set (COS) is a minimum standardised set of outcomes that should be measured and reported, aiming to increase quality and relevance of research by ensuring consistency. This study aims to identify a COS for refractory childhood epilepsy treated with ketogenic diet therapy (KDT).
Methods: Ethical approval was granted (London-Surrey REC19/LO/1680). A scoping review identified outcomes measured and reported in previous studies. Parents of a child with epilepsy treated with KDT, were interviewed to explore outcomes of importance to them. Content analysis identified all outcomes in transcripts. Outcomes were collated and grouped into domains according to the COMET Taxonomy.
Results: Of 2663 articles, 147 met inclusion criteria. 921 verbatim outcomes were sorted into 90 discrete outcomes, then classified into 21 domains. Only 52% of outcomes were reported more than once. 59% of outcomes were measured subjectively. Only 13 articles used validated tools. Parents (n=21) identified only 39 outcomes from the scoping review and 7 new outcomes including independence and participation. The long list of 97 outcomes was ratified to 77 following review and discussion with the Study Advisory Group (parents, charity, and professionals represented).
Conclusions: There is little consistency in the range of outcomes used in research. Parents identified just over a third of existing outcomes, suggesting the remainder may be less important to them. Variability in reported outcomes demonstrates a clear need for a COS for paediatric epilepsy and KDT (COMET registration #1116). Parents, professionals, and researchers are participating in a 2-round Delphi survey and consensus meeting to agree priority outcomes. The COS will guide outcome measurement and reporting in future trials and clinical practice.

Poster 035

Effect of add-on Cannabidiol (CBD) on seizure frequency and seizure-free intervals in patients with seizures associated with tuberous sclerosis complex: Phase 3 trial GWPCARE6 post-hoc analysis

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Objective: This post-hoc analysis of a randomised, placebo-controlled phase 3 trial (GWPCARE6; NCT02544763) evaluated seizure frequency reduction to determine the proportion of patients with tuberous sclerosis complex (TSC), treated with CBD or placebo, who reached all continuous responder rate thresholds and the longest seizure-free intervals.

Methods: Patients received plant-derived highly purified CBD medicine (Epidyolex®; 100 mg/mL oral solution) at 25mg/kg/d (CBD25) or 50mg/kg/d, or matched placebo for 16 weeks. Efficacy of CBD25 (n=75) vs placebo (n=76) was evaluated by percent reduction from baseline in TSC-associated seizure frequency and longest seizure-free intervals.

Results: In the 4-week baseline period, median (Q1, Q3) TSC-associated seizure frequency was 56 (21, 101) for CBD25, 54 (26, 102) for placebo; Mean (standard deviation [SD]) longest seizure-free interval was 3 (3) days for CBD25, 2 (2) days for placebo. CBD produced significantly greater reduction in TSC-associated seizures vs placebo (treatment ratio [95% CI], 0.699 [0.567–0.861]; p=0.0009). Response rates for ≥25%, ≥50%, and ≥75% reduction: 68%, 44%, and 19% for CBD25; 43%, 22%, and 0% for placebo. Mean (SD) longest seizure-free intervals: 11 (17) days for CBD25 and 6 (6) days for placebo. CBD25 vs placebo 7-, 14-, 21-, and 28-day seizure-free intervals: 45% vs 33%, 24% vs 14%, 12% vs 0%, and 8% vs 0%. AE incidence: 93% for CBD25 and 95% for placebo; 8 patients (11%) on CBD25 and 2 (3%) on placebo discontinued treatment because of an AE. Most common AEs: diarrhoea and decreased appetite, occurring more frequently with CBD than placebo. ALT/AST elevations (>3× ULN) occurred in 9 (12%) patients on CBD25 and none on placebo; 78% were on concomitant valproate.

Conclusions: CBD was superior to placebo, reducing seizures and producing longer seizure-free intervals in patients with TSC-associated seizures.

Poster 036

The highs and lows of drug resistant epilepsy and ketogenic diet therapy – a qualitative study of families' experiences

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Objective: A diagnosis of drug resistant epilepsy is life changing for a family. Ketogenic diet (KD) therapy can offer hope when other treatments have failed. However, it often requires a significant change in daily routine and dietary habits. This qualitative descriptive study aimed to explore families' experiences of epilepsy and KD therapy.

Methods: Ethical approval was granted (London-Surrey REC19/LO/1680). Parents of a child aged ≤18 years with epilepsy, currently or recently treated with KD therapy, were recruited from the UK and internationally via UK KD centres, charities, and social media. Semi-structured interviews were audio recorded, transcribed verbatim, anonymised, coded using Nvivo (V12) and inductive thematic analysis undertaken.

Results: Four themes and 12 subthemes were mapped from interviews with 21 parents (median=72mins). (1) Epilepsy is all consuming explored the impact of epilepsy on the family. (2) KD provides a window to new opportunities explores the motivators for KD therapy and positive outcomes. (3) The reality of KD explores day to day life and how families adapt to KD. (4) Looking to the future explores the factors that may make KD easier for families. Many parents described their fight to access KD therapy. KD offered parents a sense of control in an otherwise uncontrollable situation. While it presented challenges; especially in the early stages, families had creative ways of adapting and overcoming these. All were glad their child trialled KD, even when less successful. The importance of a support network including family, friends, charity organisations and the KD team was evident across all themes.

Conclusions: We conclude with five recommendations that would help support families in their management of KD therapy: improved access to KD therapy and transition to adult services, better variety and access to KD foods, ongoing support from charities, regular social education for families and finally, peer mentoring.

Poster 037

Attitudes towards, and knowledge about epilepsy among school staff

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Objective: To survey attitudes towards, and knowledge about epilepsy among school staff in a defined geographical region in the South of the England.

Methods: School staff (n=160) from 18 schools (56% of eligible schools) where children with epilepsy (4–15 years) were currently attending were surveyed. Questions focussed on attitudes towards, and knowledge about epilepsy. Factors associated with attitudes and knowledge were analysed using multivariable logistic regression.

Results: The majority of staff expressed positive attitudes towards the inclusion of children in school although a significant minority expressed less positive views. Only 30% of staff agreed that they would feel confident managing a child having a seizure whilst 42% would be concerned if they had to administer emergency medication. Regarding knowledge, only 37% of respondents were aware that all children with epilepsy do not have an Education and Health Care Plan (EHCP). Half (50%) of respondents correctly indicated that a child who has a seizure should not always leave the classroom whilst 54% knew that an ambulance should not always be called every time a child has a seizure. From a list of eight medical/neurodevelopmental conditions (e.g., asthma,

diabetes, autism, down syndrome) epilepsy was the condition staff were most concerned about. Factors independently associated with more positive attitudes and better knowledge were working in a special school, having previously witnessed a seizure and having attended training on epilepsy (all $p<0.05$). Most respondents wanted more training on seizure management and learning and behavioural aspects of epilepsy.
Conclusion: Whilst attitudes toward children with epilepsy are largely positive epilepsy was the condition school staff were most concerned about. Additionally, attitudes towards seizure management and administration of emergency medication in school are less positive. School staff in UK schools are likely to benefit from training on epilepsy in order to improve attitudes and increase knowledge.

Poster 038

Ketogenic diet in infants with epilepsy (KIWE)

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Objective: The ketogenic diet (KD) is a high-fat, low-carbohydrate diet designed to mimic the effects of starvation on the body. It has been shown in randomised controlled trials (RCTs) to be effective in reducing seizure numbers in older children with epilepsy. However, there is limited high-quality research of the efficacy of the KD in infants, where the incidence of epilepsy is greatest. KD in infants with epilepsy (KIWE) is a large scale RCT aiming to determine the effectiveness of the KD on seizure frequency compared to standard antiepileptic drug (AED) treatment in infants <2 years with drug resistant epilepsy.
Methods: Children with epilepsy (aged 1 month to 2 years) who had failed to respond to two or more AEDs were recruited across 16 sites within the UK. Participants were randomised to either the KD or further AED. Seizure frequency was recorded over 8 weeks and up to a year after intervention and compared with seizure frequency at baseline. Blood samples were also taken at baseline and 8 weeks to investigate the role of medium chain fatty acids in seizure control. Safety was monitored throughout the study.
Results and Conclusions: 136 children were recruited. 78 were randomised to the KD arm and 58 to the further AED arm. To date no adverse events have led to discontinuation of the study. Data will continue to be collected from the remaining participants until September 2021 and preliminary results are expected by January 2022.

Acknowledgements: Thank you to NIHR EME for funding the project and Young Epilepsy for providing an additional monies and support.

Poster 039

Cannabidiol for the treatment of drug-resistant epilepsy in children; a single centre experience

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Objective: The use of Cannabidiol for the treatment of childhood epilepsy has been gaining increasing interest in the recent years. In September 2019 the European Medical Agency (EMA) approved Epidyolex as an adjunct therapy, alongside Clobazam for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet Syndrome (DS) in patients ≥2 years of age. The aim of this project is to systematically observe the effectiveness, tolerability and safety of Epidyolex as an adjunctive treatment for seizures associated with LGS or DS.
Methods: This was a single-center prospective study. All patients started on Epidyolex between March and December 2020 were recruited. A standard data sheet was used to record background data, investigations results and outcome at 2, 4, 6 and 12 months. The starting dose of Epidyolex was 5mg/kg/day, which was titrated to effect thereafter. The cumulative reduction in seizure frequency was assessed at each end point.
Results: Overall, 47 patients were started on Epidyolex during the 9 months period. Epidyolex led to significant reduction in seizure frequency, 40% had 30–50% reduction in seizure frequency. 24 patients completed 12 months on Epidyolex with sustained reduction in monthly seizure frequency. The majority of patients tolerated the medication well with no significant side effects (63%). The most common adverse events included mild increase in ALT/AST (15%) and low platelets count (8%). All were on concomitant Valproate use. Sedation and GI upset occurred in 4 (10%) patients. All side effects resolved, either spontaneously while continuing Epidyolex or after reducing the dose of Valproate, Clobazam, and/or Epidyolex.
Conclusions: Treatment with Epidyolex resulted in significant reduction in seizure frequency and was generally tolerated well. In those with improved seizure control there was a relative improvement in cognition reported by the families.

Poster 040

What magnitude of reduction Is a 'clinically meaningful' change in seizure frequency? Analysis of long-term Fenfluramine phase 3 Dravet syndrome data

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Objective: A ≥50% reduction in monthly convulsive seizure frequency (MCSF) is traditionally accepted as clinically meaningful, although this threshold is largely empirically derived. Here, we

used a robust, anchor-based method in a long-term open-label extension (OLE) study of fenfluramine for the treatment of Dravet syndrome to quantify the degree of MCSF reduction associated with various caregiver and investigator Clinical Global Impression of Improvement (CGI-I) ratings.
Methods: MCSF and CGI-I data were derived from an OLE interim analysis (N=330; 19 October 2020). Correlations between MCSF and CGI-I were analyzed by Spearman's rho. Receiver operating characteristic (ROC) analysis compared change in MCSF with binary versions of investigator and caregiver CGI-I Likert scale ratings. The cut point for a clinically meaningful change, defined by ratings of 'Much Improved' or 'Very Much Improved' on CGI-I, equaled the change in MCSF where sensitivity≈specificity.
Results: Caregiver or investigator CGI data at last visit were available from 299 and 313 patients, respectively. Median treatment duration was 631 days (range, 7–1086), with a fenfluramine dose range of 0.2–0.7mg/kg/day. MCSF reduction was positively correlated with improvement in caregiver/investigator CGI-I scores (Spearman's rho, 0.530–0.545; p<0.0001). ROC analysis identified a ≥60.5% reduction in MCSF as the clinically meaningful cutoff for subjects rated as 'Much Improved' or 'Very Much Improved.' Additionally, a ≥72% reduction in MCSF was associated with caregiver/investigator CGI-I ratings of 'Very Much Improved.'
Conclusions: This analysis of the association between percent reduction in MCSF and CGI-I rated by parents/caregivers or investigators suggests that a sustained ≥60.5% reduction from baseline in convulsive seizure frequency can be considered a clinically meaningful response in patients with Dravet syndrome.

Poster 041

Experiences of clinicians, patients and carers using an asynchronous, cloud based, secure, video management platform for neurological diagnosis & care

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Objective: To explore the experiences of clinicians, patients and carers in using the asynchronous video platform vCreate Neuro for neurological diagnosis & management and inform pilot development. The platform has been utilised by >3000 patients, >400 clinicians with >8000 video uploads since 1/5/20.
Methods: Categorical questionnaires designed by clinical team and health economists with a free text option. Completed by patients/carers 5 days after video uploads and clinicians after viewing videos. Qualitative analysis of free text responses using NVivo 11 software to conduct semantic analysis and aid in identifying key themes.
Results: 621 questionnaires evaluated (375 patient/carer, 246 clinician). 174 free text responses analysed (43 clinician, 131 patient). Clinician questionnaire - video quality very high (85%) or adequate (14%), video very useful (63%) or useful (29%) to make a diagnosis, using system took shorter time to diagnose (66%) & treat (59%), ease of use - very easy (77%), easy 17%, difficult (2%). Patient/carer questionnaire - ease of use – very easy (48%), easy (39%). Does the system affect quality of care – improves (51%), doesn't affect (21%), don't know (26%). Key themes identified from free text - benefits & challenges, communication & relationships, suggestions for improvement. Sentiment analysis of clinician's comments 59% positive tone, 22% negative tone. Patients and carer's comments 44% positive tone, 53% negative tone. 10% video uploads saved a half day of schooling or work, 8% saved a whole day.
Conclusion: The service is highly valued by both clinicians and patient/carers and the vast majority find it very easy or easy to use. Free text comments from clinicians & carers informed development through the pilot phase. With novel technology patients and carers from vulnerable groups will require additional support.

Poster 042

Vagus nerve stimulation in children with refractory epilepsy – improving care

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Aims: To assess vagal nerve stimulation efficacy in the treatment of children with refractory epilepsy, from the literature and case series for service improvement.
Methods: Evidence of VNS efficacy in children was critically appraised, with emphasis on Grade 1 evidence. Retrospective case notes review of consecutive patients' response to VNS over more than 1 year was conducted to (1) Improve patient care and (2) Create a patient-centred leaflet.
Results: 3 RCTs have been performed to assess VNS efficacy (1 specific to children). These showed potential efficacy of VNS treatment. Two were industry-funded and follow-up periods were short. Blinding could not be complete due to sensation when the device is stimulating. A recent systematic review pooled data from the above and 96 non-RCTs. They reported early consideration of VNS might improve seizure outcomes and has been associated with fewer trials of medications. All studies showed that VNS is a safe and well-tolerated treatment for refractory epilepsy. We reviewed 27 consecutive cases with median follow-up of 38 months (15–72). Fifteen (55.6%) remained on 3 or more medications. 6 (22.2%)/4 (14.8%) had documentation of reduced seizure frequency/severity respectively. Four (14.8%) had documented improved behaviour since VNS treatment. Quality of life was not measured.
Interpretation: VNS is a safe treatment for refractory epilepsy. There is limited data from RCT's on its efficacy in children, but a meta analysis was supportive. Limited seizure response in our retrospective cases correlated with published studies. Poor documentation may have masked impact on quality of life (QOL) and seizure burden. Standardized tools must be used to assess/document VNS efficacy and quality of life at fixed time points. Drug reduction needs a similar approach. A patient-centred leaflet has been produced to summarise an improved pathway for patients and their families.

Poster 043

The utility of routine EEG in the diagnosis of non-epileptic attack disorder in children

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Background: Non-epileptic attack disorders (NEAD) consist of non-epileptic seizures that superficially resemble epileptic seizures

but without ictal electrical discharges in the brain. The 'gold standard' for diagnosis is a clear history, supported by video-telemetry (VT) to capture events. Capturing an event is very important and allows the question of whether this event is an epileptic seizure or not to be simply answered. Waiting for VT to confirm a diagnosis of NEAD can often lead to unnecessary delay as this investigation often encounters long waiting times.

Aim: Determine the capture rate of a typical event during routine EEG testing in children referred with a suspicion of NEAD.

Methods: Retrospective review of EEG referrals over a one-year period to a tertiary paediatric neurology department. EEG reports were reviewed on all children where the referral indicated a suspicion of non-epileptic attacks. Data collected included whether an event was captured, if it was their typical event and the type of EEG involved.

Results: There were 834 referrals for EEG during this time period. There was a suspicion for NEAD in 17 (2%) referrals during this period. Regarding these referrals (n=17), the mean age was 14 years old (range 13–16years) and 76% were female. Majority of EEGs were routine EEG recordings lasting 1 hour in duration (routine vEEG 14; prolonged vEEG 1; VT 2). 79% (11/14) of routine EEGs captured a typical event. Inter-ictal EEGs were reported as normal in 13/14 cases (93%).

Conclusions: Routine EEG is a readily available investigation that captured an event in 79% of cases in our cohort. Capturing a non-epileptic event is crucial for correct diagnosis and also for full understanding and acceptance of the diagnosis. Routine EEGs are more accessible, leading to faster identification of the correct management plan, thus avoiding un-necessary use of anti-epileptic medications and other investigations.

Poster 044

Post-neonatal epilepsy following electrographic confirmed neonatal seizures

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Objectives: To determine the incidence of post-neonatal epilepsy following electrographic confirmed seizures.

Methods: We performed a retrospective single-centre observational study of term infants at risk of seizures admitted to the NICU at Cork University Maternity Hospital between 2013–2017. Included infants were; (1) 37 weeks gestation, with (2) EEG monitoring for 12 hours and (3) had neurodevelopmental follow up. Neonatal deaths were excluded.

Results: 91 infants with neonatal encephalopathy and EEG monitoring were included. The most frequent diagnoses were HIE (62.6%), followed by genetic or metabolic encephalopathy (8.8%) and stroke (7.7%). 24 (26.4%) infants developed electrographic seizures, and 7 (7.7%) developed post-neonatal epilepsy (PNE). Of the infants with PNE, 5 (71%) had electrographic seizures in the neonatal period. Infants with neonatal encephalopathy complicated by electrographic seizures were at higher risk for PNE than encephalopathic infants who did not seize (20% vs 3%). The diagnoses associated with PNE were: epileptic encephalopathy (SCN2A mutation, n=2), tuberous sclerosis (n=1), HIE (n=2), inborn error of metabolism (IEM) (n=1) and an undiagnosed central hypoventilation syndrome (n=1). Despite HIE being the most common condition associated with seizures in the neonatal period, only 6% of infants with moderate and severe HIE developed PNE. In contrast, 50% of infants with genetic or metabolic encephalopathy developed PNE. Three infants developed epilepsy in the neonatal period (SCN2A and IEM), three within the first year, and one at 44 months. Three infants with PNE died in childhood.

Conclusions: Epilepsy is a serious neurological complication following neonatal encephalopathy. Genetic and metabolic encephalopathies were associated with the highest risk of PNE. Only two infants developed PNE following HIE. Neonatal electrographic seizures present a clear risk for PNE, particularly in infants with genetic and metabolic encephalopathy.

Poster 045

Language disorder as a distinct phenotype in sodium voltage-gated channel alpha subunit 1 (SCN1A)-related epilepsies

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Objective: Mutations in the sodium voltage-gated channel alpha subunit 1 (SCN1A) typically result in epilepsy syndromes with phenotypic variability from mild to severe neurodevelopmental presentations. Previous literature suggests co-morbid conditions are likely, including intellectual disability (ID), autism spectrum disorder (ASD), and impairments in motor, feeding, and speech domains. As a tertiary neurosciences centre seeing patients with SCN1A-related epilepsies, we sought to identify and describe the variation in neurodevelopmental presentation.

Methods: We conducted a retrospective analysis using standardised neurodevelopmental assessments following a developmental epilepsy protocol in a subset of our cohort with SCN1A-related epilepsy. Measures included cognition and adaptive function; language; social communication and behaviour.

Results: In a cohort of 16 male, 17 female, patients aged 2–13 years (median 8.75), 45.5% had severe-profound ID, 18.2% mild-moderate ID, and 30.3% were borderline-average (missing: n=2). Additional diagnoses identified were ASD (48%), ADHD (9%). Further needs identified: behaviour that challenges (24%), sleep (30%), and behavioural feeding difficulties (12%). In those with moderately impaired-average intellect (n=16) the DSM-5 diagnosis: Language Disorder was confirmed in 4 children aged 7.8–12.7 years (25%); a further 4, aged 30–42 months, were high risk for the disorder (25%). Children with language disorder were older and this impairment was not previously identified.

Conclusion: We report a distinct phenotype of language disorder in more intellectually able children with SCN1A-related epilepsies that is under-recognised in the literature. SCN1A pathogenic mutations may have a differential impact on language (separate from cognition), which may be an early marker in the developmental encephalopathy occurring in younger children. This is important as genetic therapies and other disease-modifying drugs are being trialled early in life. The phenotypic variability and late

diagnosis of language disorder in this cohort would indicate that comprehensive multi-disciplinary assessment is a necessity for all these children.

Poster 046

Comparative effectiveness of fenfluramine vs cannabidiol for the treatment of seizures in Dravet syndrome (DS): a network meta-analysis (NMA)

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Objective: Fenfluramine is a recently licensed add-on therapy to standard of care antiepileptic drugs to treat the frequent, severe seizures of DS. Although an alternative to cannabidiol, there are no comparative trials of these therapies. We assessed the comparative effectiveness of licensed fenfluramine (with/without concomitant stiripentol) to cannabidiol (with/irrespective of concomitant clobazam, per respective European/US licenses), using robust indirect comparison methods.
Method: We systematically searched for randomised controlled trials (RCTs) of licensed add-on therapies for DS. Outcomes of interest were placebo-adjusted reductions from baseline in monthly convulsive seizure frequency (MCSF), the proportion of patients achieving >25%, >50% and >75% reductions from baseline in MCSF, and the proportion of patients experiencing serious treatment-emergent adverse events (TEAEs). Comparative efficacy and safety were assessed using Bayesian NMA.
Result: For both interventions we identified two placebo-controlled RCTs. When comparing fenfluramine 0.7mg/kg/day (without concomitant stiripentol) and fenfluramine 0.4mg/kg/day (with concomitant stiripentol) versus cannabidiol (maintenance dose: 10mg/kg/day, irrespective of clobazam use) the mean differences in placebo-adjusted reduction from baseline in MCSF were 47.3% (95% CI: 18.9, 64.7), and 35.1% (1.0, 57.5), respectively. Comparing fenfluramine 0.7 and 0.4mg/kg/day to the European licensed regimen of cannabidiol 10mg/kg/day plus clobazam, the mean differences were 37.2% (2.0, 59.7) and 23.5% (-20.2, 51.3), respectively. For these outcomes, and for the proportion of patients achieving >25%, >50% and >75% reductions in MCSF, Bayesian treatment ranking indicated >98% probability that fenfluramine is the most effective therapy versus <2% probability for cannabidiol 10 or 20mg/kg/day (maximum recommended dose), with/irrespective of concomitant clobazam. Fenfluramine had lower odds of serious TEAEs, with no increase in weight loss, valvular heart disease or pulmonary hypertension versus cannabidiol.
Conclusions: NMA using RCT data indicates fenfluramine provides more effective convulsive seizure control than cannabidiol across all licensed dose regimens. Fenfluramine is comparatively well-tolerated and provides a much-needed step change in DS seizure management.

Poster 047

Impact of fenfluramine on the expected SUDEP incidence rate in patients with Dravet syndrome

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Objective: The study was conducted to compare the incidence of Sudden unexpected death in epilepsy (SUDEP) Dravet syndrome patients on fenfluramine with literature reports of SUDEP incidence of those receiving standard of care.
Methods: Relevant studies were identified by searching PubMed. Patients on fenfluramine were treated up to 0.7mg/kg/day (maximum dose 26mg/day) or 0.4mg/kg/day (maximum dose 17mg/day) if receiving concomitant stiripentol. The incidence of SUDEP was assessed using current guidelines and was expressed as deaths per 1000 person-years of observation.
Results: Nine studies were identified with the report by Cooper et al. (Cooper, M.S. et al. Epilepsy Res. 2016; 128: 43–47) considered the most rigorous. Cooper studied 100 consecutive patients with Dravet syndrome and reported an all-cause mortality rate of 15.84 per 1000 person-years (98% CI, 9.01 to 27.85) and a SUDEP rate of 9.32 per 1000 person-years (98% CI, 4.46 to 19.45). A total of 732 patients treated with fenfluramine provided 1185.3 person-years of observation. The median age of fenfluramine patients was 8 years; 89.9% were ≤18 years old at the start of treatment. Three deaths occurred—all SUDEP: one during the baseline/placebo period (11.7 per 1000 person-years) and 2 during treatment with fenfluramine (1.7 per 1000 person-years). The fenfluramine SUDEP rate was below the lower limit of the 98% CI reported by Cooper et al., whereas the SUDEP rate observed before initiation of fenfluramine was similar to the historical rate reported by Cooper et al.
Conclusions: This post-hoc analysis suggest that Dravet syndrome patients treated with fenfluramine is associated with substantially reduced risk of SUDEP and all-cause mortality compared with historical standard of care. Further research is warranted to establish the mechanism(s) responsible for this response.

Poster 048

Delineating the epilepsy phenotype in the 16p11.2 microdeletion

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Objective: 16p11.2 microdeletions are associated with a range of neurodevelopmental disorders and are a common reason for referral to clinical genetics. This microdeletion includes a number of genes including PRRT2. Loss of function variants in PRRT2 result in carbamazepine-responsive self-limited infantile seizures and PKD. In this retrospective systematic case review we aimed to assess the epilepsy phenotype of 16p11.2 microdeletion syndrome including response to carbamazepine.

Method: 62 patients had a 16p11.2 microdeletion identified by microarray. A structured casenote review was undertaken, focusing on epilepsy and developmental features.
Results: In the overall cohort, the microdeletion was de novo in 11 (17.7%) and maternally inherited in 7 (11.3%); in 44 (71%) inheritance was unknown. 14 of 62 patients experienced at least 1 seizure episode. 4 (28.6%) presented with early infantile-onset epilepsy and 2 (14.3%) with catamenial epilepsy. Seizures were self-limiting in 5 (35.7%). Median age of seizure onset was 0.92 years and median age of offset was 1.33 years. EEG was performed in 9 patients, 5 (55.6%) were normal, 3 (33.3%) revealed focal abnormalities, with 1 also displaying migrating ictal activity, and 1 generalised abnormality with photosensitivity. Anti-epileptic medications were prescribed in 7 (50%). For patients with ongoing seizures, a range of anti-epileptic medications including lamotrigine, levetiracetam and sodium valproate led to seizure reduction but not seizure freedom. Carbamazepine was prescribed for 3 patients (42.9%) who all became seizure free. In the overall cohort, 46 (74.2%) had developmental delay with 22 (35.5%) diagnosed with global developmental delay (GDD). 7 (50%) of those with epilepsy had developmental delay, with 4 (28.6%) diagnosed with GDD.
Conclusion: Carbamazepine shows potential as a targeted treatment for epilepsy related to 16p11.2 microdeletions. The delineation of the epilepsy and developmental phenotype in this study is helpful for epilepsy management, developmental surveillance and genetic counselling.

Poster 049
Everolimus for refractory epilepsy in TSC: prescribing in clinical practice according to NHS England guidance.

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Objective: Everolimus was approved by NHS England, for use in children with tuberous sclerosis complex with refractory epilepsy in November 2018. We describe clinical progress of patients in the regional TSC clinic at Evelina London Children's Hospital who have commenced on everolimus.
Methods: Case note review and clinical monitoring. Eligible patients are discussed in an MDT with colleagues in the regional epilepsy service. Formal proformas are completed to ensure criteria for treatment are met. Investigation and treatment monitoring is co-ordinated by a Clinical Nurse Specialist under Consultant guidance. Routine care includes prospective collection at baseline, 3 and 6 months post treatment of: (1) 4 week seizure diaries; (2) 1 week diary of sleep, school attendance and other activities; (3) QOL questionnaires, including Impact of Epilepsy Questionnaire and PedsQL; (4) Clinical review of patient, family impression of treatment benefit and side effects; (5) Blood monitoring according to recommended guidance.
Results: 8/13 children discussed in the MDT have commenced on treatment, one patient was in transition and is now on treatment under adult services. Twp are likely to commence treatment imminently. All 8 children who commenced remain on treatment, 7 have seen significant reduction in seizures at 6 months. 5/8 families report additional improvements in sleep, emotional regulation and quality of life, reflected in diaries and QOL measures. Side effects include: mucosal ulceration 7/8, menstrual irregularity 1/8, neutropenia 2/8, hypercholesterolaemia 2/8 (one resolved after cessation of ketogenic diet, and one spontaneously). 3/8 required temporary cessation of treatment for surgical intervention, treatment re-started with no adverse events aside from temporary reduction of seizure control, peri-operatively.
Conclusion: Everolimus for children with TSC has resulted in clinical efficacy, with manageable side effects in our population. The CNS is crucial to co-ordination of care, ensuring adherence to guidance and training staff, in the tertiary and local clinical services.

Poster 050
A retrospective study assessing seizure control in children with epilepsy under the district epilepsy service, St. George's Hospital (SGH) during 1st UK COVID-19 lockdown

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Objective: To determine whether patients' seizure control attending the SGH district paediatric epilepsy service was improved during the first COVID-19 UK lockdown period due to reduction in seizure triggering factors. At SGH, cancellation of face to face (FTF) clinics was substituted by telephone clinics during the pandemic.
Methods: Retrospective review of 255 electronic patient records under the SGH district epilepsy service. Seizure control was determined by reviewing telephone clinic letters and using a proxy measure of seizure control by assessing additional patient-initiated contacts with epilepsy consultants, epilepsy nurse specialists (EMS) and emergency department (ED) attendance.
Results: One hundred and five patients were excluded due to insufficient data on the electronic health records. Data was collected on the 150 remaining patients. Twenty-four scheduled consultant telephone clinics, 5 patient-initiated consultant contacts, 41 ENS and 7 patient seizure related ED admissions were identified. Review of clinic letters and absence of hospital contact indicated that 97 patients had good overall seizure control not requiring hospital input over that period. Reduced seizure triggering factors during the lockdown included less classroom related stress, longer overnight sleep, closer parental monitoring, better adherence to AED therapy, reduced social contacts and infection rate. Seven patients attended the ED (5 male, 1–15 years) with seizure exacerbations, 5 had poor seizure control, all had neurodevelopmental comorbidities (developmental delay, ADHD and ASD), all received monotherapy, 4 contacted SGH more than 3 times.
Conclusions: Cancellation of routine FTF clinics did not appear to adversely affect seizure outcome, whilst restrictions imposed by the pandemic resulted in reduced patient-initiated hospital contact, suggesting that the elimination of some triggering factors for epilepsy had a positive impact on epilepsy control. In future routine clinic appointments may be partially substituted by ENS led or consultant telephone clinics. Seizure related issues formed only a small number of ED attendances.

Poster 051

Perampanel for the treatment of paediatric patients in clinical practice by age category

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Objective: To assess perampanel (PER) in everyday clinical practice in patients aged <12 years.
Methods: Paediatric patients treated with PER were identified from a pooled analysis of 44 global studies. Retention was assessed after 3, 6 and 12 months. Effectiveness assessments included responder rate (≥50% seizure frequency reduction) and seizure freedom rate (no seizures since at least prior visit). Safety/tolerability assessments included adverse events (AEs). Data were analysed by age category: <4, 4–<7 and 7–<12 years.
Results: 56 patients were identified (<4 years, n=5; 4–<7 years; n=12; 7–<12 years, n=39). Retention was assessed for 41 patients in the three groups (n=2; n=10; n=29); effectiveness for 50 patients (n=3; n=11; n=36); and safety/tolerability for 47 patients (n=3; n=10; n=34). Mean PER doses at baseline and last visit (last observation carried forward) were 1.8 and 2.3mg/day; 1.8 and 4.1mg/day; and 2.1 and 4.9mg/day, in the three respective groups. Retention rates at 3, 6 and 12 months in patients aged <4 years were 50.0% at all three timepoints; corresponding rates for patients aged 4–<7 and 7–<12 years were 90.0%, 70.0% and 0%, and 89.7%, 76.9% and 63.6%. At last visit, responder and seizure freedom rates in patients aged <4 years were 66.7% and 33.3%; corresponding rates for patients aged 4–<7 and 7–<12 years were 36.4% and 9.1%, and 58.3% and 27.8%. AEs were reported for 0%, 40.0% and 38.2% of patients aged <4, 4–<7 and 7–<12 years. Most frequently reported AEs were irritability (<4 years, 0%; 4–<7 years, 10%; 7–<12 years, 14.7%) and dizziness/vertigo (<4 years, 0%; 4–<7 years, 0%; 7–<12 years, 8.8%).
Conclusions: PER was effective and generally well tolerated in this small population of paediatric patients treated in clinical practice.
Acknowledgements: Supported by Eisai

Poster 052

Fenfluramine provides clinical benefit in adults and children with Dravet syndrome: Real-world experience from the European Early Access Program

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Objective: In a recently completed phase 3 program, patients with Dravet syndrome (DS) treated with fenfluramine demonstrated sustained, profound reductions in seizure frequency, prolonged periods of seizure freedom, and improvement in executive functions. The European Early Access Program (EU-EAP) was initiated to allow pre-approval access to fenfluramine for DS patients.
Methods: Patients with a confirmed diagnosis of DS for whom seizures were not adequately controlled by their current anti-epilepsy treatment regimen and who had no alternative options (eg, other treatment, access to a clinical trial) were eligible to enroll in the EU-EAP. Fenfluramine dosing typically was started at ≤0.2mg/kg/day and was titrated based on efficacy and tolerability. Maximum dose was 0.7mg/kg/day (absolute maximum, 26mg/day), or for patients receiving concomitant stiripentol, 0.4mg/kg/day (absolute maximum, 17mg/day).
Results: A total of 150 patients with DS from the EU-EAP at multiple centers in Germany, Italy, Spain, and UK were included in this pooled analysis. The median age at the start of fenfluramine treatment was 7.2 years (range, 0.8–46 years), 49% were female, 96% had an SCN1A variant, and median exposure was 338 days. After 3 months (n=139), reductions in seizure frequency ≥50%, ≥75%, or 100% were observed in 79%, 56%, and 27%, respectively, and after 12 months (n=80), these seizure reduction thresholds were demonstrated by 80%, 51%, and 16%. Sixty-two percent were rated by the investigator as 'much' or 'very much' improved. Thirteen percent of patients have discontinued fenfluramine, primarily due to lack of efficacy. The most common adverse events were somnolence or sleep disorder (n=31) and loss of appetite (n=30). No valvular heart disease or pulmonary artery hypertension was observed.
Conclusions: DS patients treated with fenfluramine in a 'real-world' setting experienced similar benefits and tolerability as those observed in phase 3 clinical trials.

Poster 053

A retrospective audit looking at longevity of battery (IPG) life in Demipulse-103 and Aspire-106 models of vagal nerve stimulation (VNS) devices in comparison to published figures of between 3–8 years

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Summary: Vagal nerve stimulation (VNS) for medically-refractory epilepsy requires repeated battery (IPG) replacement with published IPG life of 3–8 years. We analysed which parameters had the greatest impact on IPG life to inform clinical practice and reduce frequency of IPG replacements.
Methods: Retrospective single-centre review of VNS devices that required an IPG change, totalling 15-patients (three Demipulse-103 and 12 Aspire-106 devices). Data was collected on total IPG life; normal current pulse-width, signal-frequency, and amplitude; magnet use, pulse-width, and on-time; duty-cycle; and total on-time. Additionally, data was collected on auto-stimulation in the Aspire-106 devices: total time the mode was on, average auto-stimulation per day, pulse-width, threshold, and signal on-time. The data was evaluated using ANOVA and multiple linear regression. Lead impedance was considered as a control.

Results: Mean IPG life was 3.96 years for Aspire-106 (IQR=1.03 years, SD=0.59 years) and 3.84 years for Demipulse-103 devices (IQR=0.79 years, SD=0.81 years). None of the variables under consideration significantly correlated with IPG life being over four years. However, total on-time (standardised coefficient [SC] =0.976, p=0.000, 95% CI=0.565–1.388), normal current pulse-width (SC=0.380, p=0.019, 95CI=0.079–0.680) and magnet pulse-width (SC=0.676, p=0.028, 95% CI=0.093–1.260) all positively predicted longer IPG life, while magnet signal on-time (SC= -0.936, p=0.002, 95CI=-1.440–0.432) positively predicted shorter IPG life.
Conclusion: Mean IPG life of both VNS devices lies within, however, at the lower end of the published range. A correlation was observed between IPG life and total on-time, normal current pulse-width, magnet current pulse-width and magnet signal on-time. These findings should be interpreted cautiously due to our small sample size. A larger longer-term follow-up of these patients may reveal parameters for optimising VNS-IPG efficacy-longevity balance.

Poster 054

A retrospective audit of screening for nephrolithiasis in children with complex neurodisability on zonisamide in a DGH epilepsy service

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Objective: Zonisamide is a second line or adjunctive anti-epileptic drug in children and young people (CYP) with epilepsy. Due to its action as a carbonic anhydrase inhibitor, caution is advised in those predisposed to nephrolithiasis with renal ultrasound to be arranged at clinician discretion. There is variability of practice as to who should be screened and how often. We present a retrospective audit of nephrolithiasis screening in CYP with epilepsy and complex disability treated with zonisamide.
Methods: We searched our database for all children treated with zonisamide after January 2020. Special school attendees were selected, and case notes searched for records of urine calcium:creatinine ratio and/or renal ultrasound at any time after commencing zonisamide.
Results: From our total cohort of 213 patients there were 17 patients on zonisamide, 12 of whom were in special school. Ten of these patients had renal ultrasound and 7 had calcium:creatine ratio. Four patients (33%) had evidence of renal calculi. Zonisamide was discontinued in three of these and continued with plans for repeat scan in one. Two patients had no tests; one has since discontinued zonisamide and the other did not attend for scan. Of the 5 patients in mainstream school, there were no reports of renal calculi.
Conclusions: Zonisamide treatment in complex disability has extra multi factorial risk of stone formation due to relative immobility, constipation, urine infections and fixed fluid intakes. Our small cohort includes a significant proportion that developed stones, highlighting the importance of regular screening for renal stones in CYP with epilepsy and complex disability treated with zonisamide. The role for screening in developmentally typical CYP is undetermined and consideration should be given for similar screening with topiramate use in this group. There is a need for clear regional and national guidance on this screening.

Poster 055

Interim safety data of adjunctive perampanel in patients (aged ≥1 to <24 months) with epilepsy in study 238: Treatment-emergent adverse events (TEAEs) of interest and serious TEAEs

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Objective: Perampanel is a once-daily oral anti-seizure medication for focal-onset seizures and generalised tonic-clonic seizures. We report the interim safety data from a Phase II clinical study (Study 238; NCT02914314) of adjunctive perampanel in patients aged ≥1 to <24 months with a diagnosis of epilepsy with any type of seizure.
Methods: The Core Study comprises Pretreatment (2 weeks), Treatment (12–16-week Titration; 4-week Maintenance) and Follow-up (4 weeks; for patients not entering the Extension) Periods. During the Core Study, perampanel was titrated from 0.5mg/day up to 12mg/day (patients taking non-enzyme-inducing anti-seizure medications [EIASMs]) or 16mg/day (patients taking EIASMs). Safety endpoints during the Core Study: incidence of TEAEs, TEAEs of interest and serious TEAEs.
Results: As of 29 December 2020, 20 patients were screened; 15 patients initiated perampanel treatment (mean [standard deviation {SD}] age, 14.7 [6.1] months; 66.7% female). Mean (SD) daily perampanel dose was 5.2 (2.7) mg. TEAEs occurred in 15 (100.0%) patients, of which, 11 (73.3%) patients reported TEAEs considered related to perampanel treatment. No TEAEs led to treatment discontinuation. In total, 17 TEAEs of interest were reported; the most common being somnolence (n=4) and seizure (n=3). Six (40.0%) patients reported serious TEAEs (age range: 5–23 months); no deaths occurred. All serious TEAEs occurred in only one patient except for seizure (n=3). The perampanel dose range at serious TEAE onset was 2–16mg/day, however, no patients required dose adjustments due to serious TEAEs. No serious TEAEs were considered related to perampanel treatment, and all patients recovered from their TEAEs.
Conclusions: These interim data suggest that perampanel is safe and well-tolerated in paediatric patients aged ≥1 to <24 months with epilepsy; no unexpected safety signals emerged. Enrolment of patients aged ≥1 to 6 months is ongoing.

Poster 056

Treatment with fenfluramine in patients with Dravet syndrome has no long-term effect on weight and growth

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Objective: Impact of fenfluramine (FFA) on weight gain and growth is evaluated in a long-term open-label study (OLE; Study 1503: NCT02823145).

Methods: Eligible DS patients (2–18y) enrolled in the OLE received 0.2mg/kg/day FFA starting dose and titrated to effect (0.2–0.7mg/kg/day). Z-score assessed FFA potential impact on growth at OLE baseline, Month 12, and Month 24. Z-scores were determined by the Boston Children's Hospital algorithm (height, weight, age, gender, body surface area, and body mass index). A mixed-effect model for repeated measures (MMRM) estimated change in height and weight over time.
Results: At time of analysis, FFA treated patients were 279 ≥12 months and 128 ≥24 months. For FFA patients with available data for ≥12 months, mean±SD baseline Z-score for height was -0.7±1.2 versus -0.8±1.3 at Month 12 (change: -0.1±0.4 SD). For weight, mean±SD baseline Z-score was -0.4±1.5 versus -0.8±1.4 at Month 12 (change: 0.4±0.6 SD). For patients receiving FFA ≥24 months, baseline Z-score for height was 0.7±1.2 versus -0.7±1.2 at Month 24 (change: 0.0±0.5 SD); for weight, mean baseline Z-score was -0.5±1.5, versus -1.0±1.5 at Month 24 (change, -0.5±0.7). Height and weight Z-scores were analysed by FFA dose group (0.2 to <0.3mg/kg/day, 0.3 to <0.5mg/kg/day, and 0.5 to 0.7mg/kg/day). No substantial dose-dependent changes from baseline were observed at Months 12 or 24. In MMRM, FFA patients ≥12 months treatment had an estimated change in Z-score per year for height of -0.056 and -0.166 for weight. In patients with all 3 timepoints (baseline, 12 months, and 24 months; n=110), estimated changes in Z-scores per year were -0.025 for height and -0.188 for weight. Differences in Z-scores for height and weight were minimal over time (FFA patients treated for ≥12 months (n=262) and ≥24 months (n=110)).
Conclusions: Long-term treatment with fenfluramine had minimal impact on DS patients' growth.

Poster 057
'Seven at one blow' A Brum tale- health education to families of children with epilepsies, sharing a tertiary centre experience

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Background: Patient education is a central component of any chronic condition. Families of children with diagnosis of epilepsies are educated on their condition, acute management of seizures and medications prescribed at diagnosis and follow-up. Families are usually frightened and overwhelmed at diagnosis. Health education is vital to get back the control and to adjust to the changes in their life.
Objective: To develop a tool to support and facilitate effective epilepsy education.
Methods: We introduced an epilepsy information hour for the families of children with epilepsies. The evening was organised on a virtual platform. We sent out 60 invites along with a pre-event questionnaire. That questionnaire led to identification of knowledge gap and hence appropriate sessions. In the hour there were 5 brief presentations on acute management of a seizure, local epilepsy services, pill club, transition and sudden unexpected death in epilepsy (SUDEP) along with time for questions and discussions. We assessed the effectiveness of the information hour with votes on the day.
Results: 25 invited families attended the meeting. The pre-event questionnaire showed that only 66% families knew how to contact epilepsy team in the hospital. Only 61% of families had heard of the term SUDEP. 10% of the families were unsure what to do in the event of an acute epileptic seizure. The votes at the end of the event showed that 96% of families knew how to contact the epilepsy team, what to do in the event of epileptic seizures and all the families were introduced to the term SUDEP. Families sharing their experience provided support for other parents and gave health professionals a better understanding of the disease impact.
Conclusion: This epilepsy information evening proved to be an effective means to support and facilitate epilepsy patient and family education.

Poster 058
Lacosamide- as a treatment option in SCN8 related epilepsy

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Introduction: Sodium channelopathies are one of the better recognised genetic channelopathies. Aggressive seizure control must be pursued to reduce risk of sudden unexpected death in epilepsy (SUDEP) in these children. In addition to traditional anti-epileptic drugs (AED), Lacosamide should be considered as it has the unique ability to interact with sodium channel slow inactivation without affecting fast inactivation.
Case Report: A 10-year-old girl was seen in the epilepsy clinic due to refractory epilepsy with high seizure burden. She presented at 1 year of age with afebrile generalised tonic clonic seizures. She was born at term with no complications and family history of epilepsy and later received a genetic diagnosis of SCN8A related epilepsy and failed seizure control with multiple medications. She was started on Lacosamide after discussion with parents and shortly after became free of any convulsive seizures.
Discussion and Conclusion: SCN8A pathogenic variants have been associated with developmental delay prior to and/or after onset of seizures, intellectual disability without seizures, and epileptic encephalopathy with multiple seizure types. It is essential to be familiar with the pharmacotherapy for SCN8A-related epilepsy with encephalopathy and how it differs from treatment of similar disorders like Dravet syndrome. The predominant mechanism underlying epileptic encephalopathy appears to be neuronal hyperexcitability caused by gain of function variants and studies suggest that these patients respond favourably to the class of AEDs that block sodium channels. In contrast to other AEDs, Lacosamide facilitates slow inactivation of sodium channels both in terms of kinetics and voltage dependency. This effect may be relatively selective for repeatedly depolarized neurons, such as those participating in seizure activity in which the persistence of sodium currents is more pronounced and promotes neuronal excitation and was the biological basis for consideration of Lacosamide in this patient. We stress the importance of targeted AEDs in genetic epilepsies to improve patient outcomes.

Poster 059

Cannibinoids as a treatment option in CASK associated epilepsy

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Objective: This case reports the use of cannibinoids as a treatment option for CASK associated epilepsy. Around 50% of patients with CASK mutations have epileptic seizures with variable clinical and electrographic appearances. In females, seizures commonly present as epileptic spasms with onset occurring after 1 year of age. Males present earlier with developmental and epileptic encephalopathies. Seizures are typically challenging to treat with drug resistant epilepsy seen in up to 50% of patients and no specific treatment available.
Methods: We reviewed the case notes, EEG, laboratory findings and MRI reports for patients at our institution with CASK associated epilepsy.
Results: We present a female with developmental delay from 3 months of age and seizures from 4 years old. MRI showed marked cerebellar volume loss with widening of the 4th ventricle and brainstem hypoplasia. Genetic analysis confirmed a CASK mutation. Her seizures initially manifested as tonic neck extensions and abnormal eye movements. Subsequently myoclonic jerks, absences and motor seizures were reported. Aged 9 years old episodes occurred up to 100 times per day. From sleep they presented as 'whole body tonic shocks' occurring in clusters lasting up to 15 minutes. Daytime episodes consisted of head drops multiple times an hour. EEG recording captured the habitual epileptic spasms and demonstrated almost continuous epileptiform discharges and generalised prolonged runs of 1 to 2 Hz spike and slow wave activity supportive of a diagnosis of Lennox Gestaut Syndrome. Trials of phenobarbitone, lamotrigine, ethosuximide and clobazam were unsuccessful. Initiation of cannabinoids (Epidyolex 5mg/kg/d) with clobazam led to a dramatic cessation of seizure activity with 48 days seizure free at last review.
Conclusion: Cannibinoids have shown promise in this patient with CASK associated epilepsy. Further study of targeted anti-epileptic drugs for this group of patients is warranted.

Poster 060

Early morning headaches as a post-ictal manifestation: let's be open-minded

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Objective: We report the case of a child presenting with early morning headaches and discuss the underlying diagnosis.
Methods: We reviewed and analysed data from the electronic patient record and the EEG database.
Results: Our patient is a 10-year old female, previously fit and healthy with normal development. At the age of 9 years she had a generalised tonic-clonic seizure, lasting 5 minutes and self-resolving, while co-sleeping with her mother on the sofa. She has not been observed to have any further seizures. She presented to us a year later with a 3-month history of gradually worsening, early morning headaches sometimes associated with vomiting. Although not initially reported, when asked, she admitted that she may intermittently experience brief episodes of blurry vision. No previous history of headache was present. Neuroimaging, cerebrospinal fluid investigations and ophthalmological evaluation were normal. Given the history of unusual early morning headaches and vomiting, we performed a sleep EEG, which revealed diffuse epileptiform discharges (spike and wave activity) with occipital predominance and fixation off sensitivity. During sleep, epileptiform activity increased without reaching Electrical Status Epilepticus during slow wave sleep threshold. Diagnosis of self-limiting occipital epilepsy of childhood (Gastaut type) was, therefore made. Despite the self-limiting course of this entity, given the burden of symptoms of daily morning headaches, our patient was started on levetiracetam and since then she has been free of symptoms (headaches/vomiting).
Conclusions: Peri-ictal headaches represent a well-known ictal or pre-/post-ictal manifestation, especially in patients with occipital epilepsies. It is quite likely that our patient had subtle unreported seizures in sleep. However, isolated early morning headaches as the only post-ictal manifestation of seizure activity during sleep have not been previously described in that type of epilepsy. Our case highlights the need to be open-minded when evaluating children with atypical neurological symptoms and think beyond obvious causes.

Poster 061

Audit of the concordance of teenagers with epilepsies with their antiepileptic drug treatments

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Objective: To measure the concordance of teenagers with epilepsies with their antiepileptic drug (AED) treatments.
Methods: We created a questionnaire for patients attending the teenage epilepsy clinic. Simple descriptive statistics were used. This was a registered clinical audit (21–102C).
Results: 39 patients aged 13–18 years (median 16) were included, 17/39 (44%) with generalised and 21/39 (54%) focal epilepsies. 27/39 (69%) were taking one and 12/39 (31%) two AEDs. During the previous month, 22/39 (56%) reported no missed doses: concordance score (CS) 6/6; 14/39 (36%) 1–5/60: CS 5/6; and 3/39 (8%) 6–10/60 missed doses: CS 4/6. Among the patients reporting the best CS 6/6: 12/22 (55%) were taking one and 10/22 (46%) two AEDs; 15/22 (68%) had an AED dose between 25–74% of top of target dose range for the first AED and 5/22 (23%) had AED dose more than 75% of top of target dose (this was 4/10 (40%) and 2/10 (20%) for the second AED); 17/22 (77%) had >90% reduction of their seizures, 4/22 (18%) had 50–90% reduction; and 1/22 (5%) had more than twice as many seizures. Among the patients reporting a poor CS 4/6: all 3 were on one AED, 2/3 had an AED dose between 25–74% of top of target dose range and 1/3 had an AED dose more than 75% of top of target dose; none were seizure free nor had a seizure reduction >90%, 2/3 had a seizure reduction between 50–90%, and 1/3 (33%) had less than 50% reduction of their seizures.
Conclusions: Among our patients, most reported good concordance with AED treatment. Best concordance was associated with good seizure control whereas none of the patients with the worst concordance had a >90% seizure reduction. More data will be collected to confirm these preliminary impressions, and validate the CS method.

Poster 062

Micturition and defecation induced reflex seizures in a child with post NMDAR encephalitis

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Although acute symptomatic seizures are a known presentation of anti-NMDAR encephalitis, little is known about the risk of developing chronic epilepsy in children. Micturition and defecation triggered reflex seizures are rare and have not been described in patients with post anti NMDAR encephalitis. We describe an 8 year old male with drug resistant epilepsy due to anti-NMDAR encephalitis who along with unprovoked nocturnal seizures had micturition and defecation triggered reflex seizures. He initially presented with status epilepticus, movement disorder, challenging behaviour and encephalopathy and was treated with steroids, IVIG, plasmapharesis and antiepileptics. He also had neurogenic bladder managed with prolonged catheterisation contributing to urinary tract infection in the acute phase. He recovered remarkably except for persistent cognitive concerns and recurrent unprovoked seizures treated with Carbamazepine and Levetiracetam and Mycophenolate mofetil for 2years. His nocturnal seizures still persisted and six months thereafter had recurrent micturition triggered seizure initially and later provoked by defaecation too. These were characterized by flexion over abdomen while sitting in the toilet usually midway during voiding. Then he fell towards a side with dystonic posturing of hands, hyperkinetic movements of legs, had fearful nonverbal vocalisation with hyperventilation lasting 10–20 seconds. Relapse was excluded by negative blood and CSF antibody titres. Persistent bilateral residual claustral changes were noted on neuroimaging. MRI spine, urine examination and urodynamic studies were unremarkable. EEG showed rhythmic notched theta delta activity over the right centrotemporal regions. The antiepileptic drug therapy was optimised and the triggered seizures gradually subsided over the next 9 months although nocturnal seizures persisted. A rare case of post NMDAR encephalitis with drug resistant epilepsy with micturition and defecation triggered seizures is highlighted which shows that chronic epilepsy might potentially result from irreversible changes that alter neuronal networks and persist even after the inflammatory process resolves.

Poster 063

Major motor drop seizures for endpoint assessments in a phase 3 trial of soticlestat in individuals with Lennox–Gastaut syndrome

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Objective: Clinical trials for the treatment of Lennox–Gastaut syndrome (LGS) typically include drop seizure assessment as an efficacy outcome measure. However, drop seizures may be difficult to identify by parents/caregivers given that they are usually brief, may not involve an actual drop, and may involve either the whole body, just the head, or other body areas. Inconsistent seizure assessment can cause variability in clinical trial data. An outcome measure should be clinically relevant, easily identifiable, and reliably counted across study sites. Soticlestat, a first-in-class cholesterol 24-hydroxylase inhibitor, is being investigated as adjunctive therapy for children and adults with LGS and Dravet syndrome. To reduce potential variability in drop seizure assessments in upcoming phase 3 studies in LGS, we sought to develop a new operational definition for drop seizures.
Methods: As part of the phase 3 clinical study protocol design, in consultation with researchers in the epilepsy field and epileptologists, and considering the International League Against Epilepsy (ILAE) seizure classification, an updated term for drop seizures was developed.
Results: The term 'major motor drop' (MMD) seizure will be used as the primary efficacy outcome measure in a phase 3 study of soticlestat in individuals with LGS, and as a secondary outcome in the associated open-label extension study. MMD seizures will be identified based on ILAE seizure classification categories and the body areas involved. Focal-onset, generalized-onset and unknown-onset motor seizures that involve the major body areas and do, or could, lead to a fall, will be considered MMD seizures. Motor seizures such as isolated head drops or involving only the face and arms will not be considered MMD seizures.
Conclusions: Using the MMD seizure definition in the clinical trial setting may lead to a more accurate and reliable measure of the efficacy of antiseizure medications for the treatment for LGS.

Poster 064

Atypical presentation of microcephaly-capillary malformation (MIC-CAP) syndrome

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Autosomal recessive microcephaly-capillary malformation (MIC-CAP) syndrome is described in only 18 individuals to date (March 2021). Features described include profound microcephaly, multiple cutaneous capillary malformations, hypoplastic distal phalanges, early onset refractory epilepsy and significant developmental delay. Here we describe a case with atypical features that expands the clinical spectrum. Our patient, now aged 12 years, presented with neonatal onset global developmental delay and visual impairment. Aged 10 months she developed refractory prolonged seizures with intercurrent illness. These evolved to include asymmetric tonic seizures with apnoeas, right-sided focal seizures, focal seizures involving looking scared and swallowing, and tonic-clonic seizures. She now has episodes of eye fluttering and behaviour change, but it is not yet clear if these are epileptic. She has no cutaneous capillary malformations and digits are normal. Her head circumference is on the 0.4th centile. She is profoundly neuro-developmentally impaired.
Investigations: Serial MRI brain imaging shows symmetrically small hippocampi and optic nerve hypoplasia; both previously described. However there is no progressive atrophy or abnormal myelination. Compound heterozygous variants in the STAMBP gene were identified through the Deciphering Development Disorders (DDD) study and Western blot analysis of a lymphoblast cell line

subsequently confirmed the absence of STAMBP protein. Our patient has been investigated for alternative diagnoses with metabolic investigations (organic acids, amino acids, biotinidase), EEG, renal USS, Ophthalmology assessments and genetic investigations (array CGH and whole exome sequencing). Echocardiogram showed a small ASD.
Conclusion: MIC-CAP syndrome is extremely rare. This case highlights an atypical clinical phenotype. Our patient does not have profound microcephaly, neonatal onset seizures or anomalous digits. Most notably, one of the defining hallmarks of the condition, capillary malformation, may not always be present. Therefore, in cases such as ours, it may be more appropriate to make a diagnosis of 'STAMBP-related neurodevelopmental disorder' rather than MIC-CAP syndrome.

Poster 065

UNC-80 gene mutation causing early infantile epileptic encephalopathy in a child with trisomy 21: case report

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Case presentation: We report a 3-year-old female with Trisomy 21 and epileptic encephalopathy. She was the first child of consanguineous parents who were of Asian origin. She was born at 35 weeks of gestation by C-section and had chronic lung disease needing home oxygen treatment. She had dysmorphic features that are consistent with Downs Syndrome. She had profound global developmental delay (not able to sit independently), hypotonia, poor growth, convergent squint, central sleep apnoea, reflux and laryngomalacia. She also had a history of recurrent aspiration. MRI Brain revealed mild generalised atrophy and signal changes in the basal ganglia. Her seizures and gross developmental delay were not explained by the underlying diagnosis of Trisomy 21. Further genetic testing with exome sequencing led to the identification of a homozygous mutation in UNC80 gene.
Background: The NALCN gene encodes a voltage-independent, non-selective, cation channel which conducts a permanent sodium leak current and regulates the resting membrane potential and neuronal excitability. It is part of a large channel complex, consisting of multiple proteins including UNC80 and UNC79. The UNC80 gene is essential for the stability and function of the NALCN sodium leak channel and for bridging NALCN to UNC79 to form a functional complex. Homozygous or compound heterozygous mutation in the UNC80 gene are associated to the IHPRF2 syndrome (Infantile hypotonia with psychomotor retardation and characteristic facies).
Conclusion: The range and severity of the medical problems out of keeping with the primary diagnosis should prompt investigation for an additional diagnosis, especially in consanguineous families. Genetic testing via extended gene panels, whole exome and whole genome testing is more likely to yield a definitive diagnosis in these patients. Early diagnosis is key for optimising the care of these patients as well as for genetic counselling for further children.

Poster 066

Neonatal refractory status epilepticus due to autosomal recessive novel variant in the SLC13A5 gene

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Objective: To describe the clinical presentation, investigations, and management of a child with neonatal refractory status epilepticus due to autosomal recessive novel variant in the SLC1A35 gene and literature review.
Methods: Review of case notes and literature.
Results: 16-day old baby presented with recurrent seizures characterized by mouthing, generalized tonic stiffness with jerks and drowsiness in-between episodes over the last day. She had neonatal seizures on day-2 which had responded to levetiracetam and phenobarbitone Initial EEG showed an abnormal background with burst suppression pattern which partially improved with intravenous pyridoxine. Two clinical seizures were associated with left temporo-occipital spike and wave spreading to the right side. Intravenous phenobarbitone, levetiracetam and fosphenytoin were given with incomplete response. Hence Pyridoxine, Pyridoxal-5-phosphate, Folinic acid and Biotin were added. Day-18 MRI Brain showed T2 ill-defined patchy hyperintensities in the subcortical and deep white matter of the frontal and parietal lobes suggesting metabolic etiology. Phenobarbitone and levetiracetam were stopped on day-19 as child was seizure free. Child was discharged home on day-21 on oral phenytoin and vitamin supplements. Day-28 seizures recurred, doses of phenytoin were adjusted with levels, clobazam was added. Clinical exome sequencing showed homozygous nonsense variation of exon5 of SLC13A5 gene c.682G>T (p. Gly228Ter). Bioinformatic analysis indicates the pathogenicity of the mutation. Hence vitamins were stopped, carbamazepine was added. Child remains seizure free on carbamazepine and clobazam and is weaning phenytoin. Literature review indicates mutations in SLC13A5 are associated with seizure onset during the first days of life, progression to recurrent and refractory epilepsy with frequent status epilepticus. This child has a novel variant.
Conclusion: This child with a novel mutation in the SLC13A5 gene presented as neonatal refractory status epilepticus with response to fosphenytoin. Though MRI Brain and EEG suggested a metabolic aetiology, elucidating genetic diagnosis has helped with treatment of seizures.

Poster 067

Siblings with trisomy 8q24 due to an unbalanced reciprocal translocation with neurodevelopmental problems and valproate-resistant epilepsy

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Patient characteristics: A 3-year male presented with generalised tonic-clonic seizures. He was the first child to unrelated parents. He continued to have frequent seizures and his EEG showed generalised spike and wave activity. He also had

neurodevelopmental problems, including speech and language delay, attention deficit and autism. His younger sister presented at the age of 1 year with myoclonic jerks and absence seizures. Her EEG showed generalised epilepsy with myoclonic absences. Her developmental milestones were delayed. Both children's epilepsy was resistant to treatment with Sodium Valproate but responded well to a combination of Levetiracetam and Lacosamide.

Investigations: The proband's father carried an apparently balanced reciprocal translocation between the subtelomeric regions of the short arm of one chromosome 2 and the long arm of one chromosome 8. His karyotype was 46,XY,t(2;8)(p25.1;q24.13). Chromosomal microarray on the male child showed an unbalanced chromosomal rearrangement due to malsegregation of his father's apparently balanced reciprocal translocation. He had a gain of a 10.9Mb region at 8q24.22q24.3 and loss of a 52Kb region at 2p25.3. The 8q24.22q24.3 duplication had resulted in the child having additional copies of 103 protein-coding genes, whereas the 2p25.3 microdeletion had resulted in loss of a single protein-coding gene (FAM110C). His younger sister had the same unbalanced chromosomal translocation.

Discussion and Conclusions: The 8q24.22q24.3 duplication is the likely cause of the epilepsy and neurodevelopmental problems in the siblings. There are previous reports of children with overlapping 8q24 duplications with similar neurodevelopmental problems, including epilepsy. The much smaller 2p25.3 microdeletion is not thought to contribute to their phenotype as it is a frequently seen polymorphism in the general population. In addition, no phenotype has been linked to the FAM110C gene. These siblings demonstrate that epilepsy due to 8q24 duplication may be resistant to treatment with Sodium Valproate.

Poster 068

Case report of extreme bone fragility in a child with ARX gene related epileptic encephalopathy

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We report a 3-year-old male with Otahara syndrome with de novo ARX gene mutation (ARXc.1471 dup p(leu491Profs*41) and extreme bone fragility. He has recurrent fractures of femurs, tibia, metatarsals, ribs and spine and very low bone density despite regular pamidronate infusions. He has neonatal onset epileptic encephalopathy (Otahara syndrome) with multiple seizures daily. Treatment include sodium valproate, lacosamide and clobazam. Classical ketogenic diet continued since age 5 months with regular biochemical monitoring and Liquigel and Calogen supplementation. His bone profile, vitamin D and PTH remained normal, with no acidosis, tubulopathy or renal phosphate wasting. He has severe developmental delay and hypotonia with no dystonia. MRI brain is normal. No further abnormalities detected in epileptic encephalopathy panel (including SCN2A and SCN8A mutations) or extended osteogenesis imperfecta panel. Antiepileptic medications reduce bone mineral density via CYP450 isoenzymes induced vitamin D deficiency, hyperparathyroidism and direct bone resorption. Studies show 9–21% incidence of fractures in children with resistant epilepsy treated with ketogenic diet and multiple antiepileptics. Ketosis and acidosis induced low vitamin D and growth factors lead to osteopenia. Epileptic encephalopathy and severe bone loss are reported with several gene mutations (i.e SCN 8A mutation). ARX gene expressed in brain, skeletal muscle and liver is not associated with bone fragility except with renal phosphate wasting. Hence he manifests extreme bone fragility due to his epilepsy and its treatments. This may be a rare case of ARX gene related osteoporosis, or he has a yet unidentified genetic explanation, the whole genome sequencing may uncover. Biochemical monitoring during ketogenic diet and supplementation varies across UK. Current expert consensus guideline recommends DEXA scans 2 years after starting ketogenic diet. Uniform bone health monitoring and supplementary practices might be helpful in children with early onset epilepsy. Reporting this case may bring to light similar experiences.

Poster 069

NEXMIF-mosaic variant in a female with drug resistant genetically generalised epilepsy

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Introduction: Pathogenic variants in NEXMIF (neurite extension and migration factor) cause an X-linked developmental and/or epileptic encephalopathy. Males have significant ID, autism, and dysmorphism. We report a female patient with a mosaic heterozygous NEXMIF variant and idiopathic/genetically generalised epilepsy.

Case Report: An 8y-old female presented with absence seizures, some prolonged (1–2 minutes) and some associated with slumping/drops, initially responsive to sodium valproate with only occasional seizures for 4 years. EEG at onset showed frequent generalised epileptiform activity with polyspikes. Aged 13y epilepsy evolved to a predominant phenotype of eyelid myoclonia (daily), having several emergency presentations with clusters of eyelid myoclonia, absences and trunk myoclonia requiring emergency treatments. Seizures were resistant to the addition of levetiracetam. Repeat EEG showed frequent generalised bursts of polyspike, and paroxysms with eye-closure. Ethosuximide addition led to excellent control, and general wellbeing with marked improvement of EEG discharges. Due to attention difficulties, dyslexia and slightly low set ears, epilepsy gene panel testing was performed, identifying a mosaic pathogenic NEXMIF variant (c.964C>T; p.Arg322). Early and family histories were unremarkable.

Discussion: Females with pathogenic variants in NEXMIF can range from unaffected to drug-resistant epilepsy. Random X-inactivation is hypothesised to explain the variation of phenotypes in females. This is this is the first case of NEXMIF-related IGE/GGE in a female with mosaicism. The GGE consisted of frequent absences, eyelid myoclonia, occasional drops and body myoclonia, and responded well to combination of valproate and ethosuximide. The variant, not reported in mosaicism previously, has been described in 1 severely affected male (expectedly) with no seizures, and 2 females with drug resistant epilepsy and moderate ID (without reported skewed distribution of X-inactivation). Epilepsy gene testing should be considered in drug resistant IGE/GGEs including those with eyelid myoclonia/Jeavon's syndrome, subtle dysmorphism or developmental concerns, due to very important treatment and genetics counselling implications.

Poster 070

Double trouble: co-occurence of CACNA1A and NEXMIF variants in epilepsy

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Objective: With the widespread use of next generation sequencing for epilepsy and developmental delay, an increasing number of variants are discerned in each patient. We present an illustrative case example of 'double trouble', where the interpretation of potentially pathogenic variants was further challenged by variable penetrance and expanding phenotypes in these, and many other, epilepsy genes.
Methods: Analysis of next generation sequencing (NGS) panel data, case-note and literature review.
Results: The proband is an 11 year old female with intellectual disability, autism spectrum disorder and pharmacoresistant epilepsy. Her mother has intellectual disability; and father has intellectual disability, ADHD and seizures. Her seizure onset was at 2y, with absence seizures. She subsequently developed eyelid myoclonia and limb jerks, followed by drops. She is currently on three anti-seizure medications. She is overweight (>99.6th centile), does not have distinctive facial features and has essentially normal neurological examination. MRI brain and neurometabolic work-up were normal. EEG was very abnormal with widespread high amplitude spike/polyspike and slow wave discharges over both hemispheres and with a left sided bias. Microarray and Fragile X-testing were normal. A NGS panel revealed Class 5 pathogenic variants in NEXMIF: c.1882C>T p.(Arg628*) and CACNA1A c.2847_2856del p.(Ala952Serfs*115). Phenotypic features of the recently described X-linked NEXMIF encephalopathy include developmental delay/intellectual disability, autism spectrum disorder, and epilepsy. Males have more severe developmental impairment, whereas females show wide phenotypic diversity, ranging from completely asymptomatic to severe intellectual disability and pharmacoresistant epilepsy. CACNA1A channelopathies have been implicated in developmental delay, autism spectrum disorder, epileptic encephalopathy and early onset paroxysmal dystonia, in addition to the typical episodic ataxia.
Conclusions: This case highlights the difficulty of variant interpretation in composite phenotypes in the genomic era. Further phenotyping and testing of the extended family is ongoing and will have implications for disease surveillance and genetic counselling.

Poster 071

Emergency healthcare utilisation by children with epilepsy

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Objective: We set out to measure the frequency of emergency healthcare utilisation of a cohort of children with epilepsy looking at both epilepsy and non-epilepsy related admissions.
Methods: All children with epilepsy in the area are known to the local team and their details were obtained through the departmental database. We studied the children's attendance to ED and admissions to the paediatric ward over a twelve month period from 01/01/2020 to 31/12/2020.
Results: 134 children with epilepsy between the ages of 0–16 years of age were known to the local paediatric team. Sixty one (45.5%) sought emergency treatment at least once over the study period. Twenty four (17.9%) episodes were due to an epilepsy related issue whilst 37 (27.6%) were due to a non-epilepsy related issue.
Total number of attendance was 110 (820/1000 children). The commonest reasons for presentation were trauma and increased seizure activity. Fifty five episodes (50%) led to an admission to hospital.
Seven admissions with status epilepticus (3 different patients) and 3 admissions with side effects from antiepileptic medication. Two PICU admissions with respiratory issues. No deaths.
Published data from Northern Ireland (1) shows an ED attendance rate of approximately 300 per 1000 children and an admission rate of approximately 15%
Conclusion: Children with epilepsy have a higher level of emergency healthcare use and admission to hospital than non-epileptic children, which is not just related to seizure control. There was a high level of ED attendances due to trauma. Some of these may have been secondary to unrecognised seizures or unsteadiness due to AEDs but it may also show an increased willingness of parents with children who regularly attend the hospital epilepsy service to seek hospital treatment with more minor problems.

Poster 072

Seeking out the sun: A case of sunflower syndrome

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An 11-year-old female with no significant perinatal, developmental or family history, presented with a 2-year history of episodes of bringing hands in front of her face and with fingers spread wide apart, waving them in front of her eyes. This was then followed by eye fluttering and on certain occasions progressing to tonic-clonic movements with loss of tone. These episodes would always occur on exposure to bright sunlight or LED lights. There was a striking history of increasing frequency of episodes during sunnier seasons and during holidays at sunnier places. For the first couple of years after presentation, she was diagnosed with tic disorder. It was only when she developed tonic-clonic movements that epilepsy was suspected and EEG was done which demonstrated clear evidence of photosensitivity with photo-paroxysmal response and evidence of generalised epilepsy manifested by bicentral spike and slow wave activity. The stereotypical hand waving triggered by exposure to sunlight and the EEG findings led to the diagnosis of Sunflower syndrome. She was started on sodium valproate which led to significant improvement. This case serves to highlight the importance of increasing awareness about Sunflower syndrome, a rare type of childhood onset generalised epilepsy with photosensitivity. It is characterised by typical semiology of hand-waving episodes triggered by exposure to light and photosensitivity. The light-induced seizures usually manifest as eye fluttering and can be easily misdiagnosed as tics or eye motor stereotypies. Diagnosis is especially important as reduction in seizure frequency can be achieved with antiepileptic drugs and

non-pharmacological measures including avoiding stimulus, focusing on other tasks and use of hats and sunglasses.

Poster 073

[THIS POSTER HAS BEEN WITHDRAWN.]

Poster 074

Epilepsy treatment and cognitive function in Nigerian children: A comparative cross sectional study of children on carbamazepine, valproate and levetiracetam monotherapy

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The choice of anti-epileptic medications for treatment of seizures in children usually requires a trade-off between side effect and efficacy. Adverse effect of anti-epileptic drugs (AEDs) may be partly responsible for cognitive impairment in CWE on AED treatment. The effect of AEDs on the cognitive performance of Nigerian CWE is not known. The aim of this study was to determine if drug-specific difference in cognitive performance occur Nigerian CWE on monotherapy with three common AEDs (carbamazepine, valproate and levetiracetam).
Method: The participants comprised of 54 children with idiopathic epilepsy (20 on carbamazepine monotherapy, 16 on valproate and 18 on levetiracetam monotherapy) aged six to 16 years who were on AED treatment for six months or more and seizure free for at least three month. Cognitive assessment was done using the Wechsler intelligence scale for children (fourth edition) and the Iron psychology computerized test battery.
Result: The mean age of the sample population was 10.63years (+/- 2.99years). Twenty eight (51.9%) were males and twenty six (48.1%) were from the lower socio-economic class. The three groups had comparable scores on test of Intelligence (F-0.524, p-0.595); Attention (F-2.354, p-0.105); Verbal memory (F-0.408, p-0.667); Visual memory (F-1.882, p-0.163); Tapping task (F-0.246, p-0.782); auditory reaction (F-0.077, p-0.926) and visual reaction (F-0.418, p-0.661).
Conclusion: There is no difference in cognitive performance of CWE on monotherapy with carbamazepine, valproate and levetiracetam.

Poster 075

Innovative effort to digitally transform paediatric epilepsy care using 'Patients Know Best' at a district general hospital in UK

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Patients Know Best (PKB) is a digital platform developed by independent social enterprise that supports NHS by sharing information with patients in a secure way. This enables patients to have a better understanding of their care empowering them to become the drivers of their own health outcomes.
*Objective*s: By building a single digital patient held record the project team aimed to empower parents of children and young adults with epilepsy to hold and monitor their own health information, contact epilepsy team, have access to reports and letters, access to library of paediatric epilepsy information and share videos and diary of seizures with professionals.
Method: Between June 2020 and July 2021, a team of paediatric epilepsy professionals working across community and hospital developed the project building contents of digital platform utilising the existing application on PKB modifying for epilepsy care, monitoring the outcomes using PDSA (Plan, Do, Study, Act) method while incorporating the improvements at each stage. Parents of complex epilepsies ad young adults were involved in building the content. The key components of the digital platform are a readily available secure digital record of patient information on any web-linked device, enabling two-way communication between parents and professionals including videos, patient entered seizure diary, library of medical information related to epilepsy and intention to integrate platform with all hospitals and GP records. The project is at pilot stage and will be extended to entire epilepsy patient population at next stage.
Results: Parents and young adults who were recruited in pilot stage have readily approved the PKB digital platform and were also involved in co-designing some of the components. We will share the experience and outcomes individual case reports at the conference including the features of the project.
Acknowledgements: Luton Clinical Commissioning Group for securing funds from NHS England.

Poster 076

CHECC - Child and Young person Epilepsy Concerns Checklist. A holistic epilepsy and wider needs screening tool

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The CHild and young person Epilepsy Concerns Checklist (CHECC) has been developed with feedback from professionals, families and charities specifically to identify and support the wider and more general needs of CYP with epilepsy. This aims to promote a systematic approach whilst attempting to minimise the burden of using a large number of screening tools and questionnaires for each individual with epilepsy. Carer, young person and school/nursery versions have been developed to include neurodevelopment, emotion and behaviour concerns as well as safety, general health transition and goal setting. Areas of concern should be further explored in sufficient detail to help guide decisions about further evaluation or treatment. Ideally all items should be completed to avoid overlooking a particular area of concern or need.
We present the results from this pilot tool based on 15 children with the CHECC completed by their teachers. Emotional or behaviour concerns were reported in 7, social interaction and/or communication concerns in 9, attention and concentration and learning concerns were reported in 9. There were no reported concerns re safety, supervision or care plans. All of the 7 respondent who gave feedback indicated that the questionnaire was the right length. This pilot study indicates that he CHECC may be an acceptable and effective tool for collating education professional concerns about the child or young person with epilepsy.

Poster 077

Feasibility pilot of virtual acceptance and commitment therapy (ACT) groups for adolescents with epilepsy

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Introduction: The aim of this feasibility pilot was to develop and adapt an ACT group for adolescents with epilepsy for virtual delivery in the context of Covid-19 restriction. The psychological theory and strategies used as part of the group content was based on an ACT approach and its efficacy in chronic health settings.
Method: A virtual platform was used to deliver five weekly 1.5 hour sessions to adolescents aged between 12–17 years living with epilepsy. The CompACT and Peds-QL (Teenager) were used to collect quantitative outcome data. We received 18 referrals across two groups; one in July 2020 and one in January 2021. 11 adolescents attended the group in total with the mean age being 15.18 years.
Results: Across attendees who completed both pre and post measures (N=2), psychosocial health scores improved by 29%, and psychological flexibility scores improved by 46% following completion of the group. The group was described as 'friendly', 'helpful', 'informing' and a 'sense of community' during qualitative feedback collection.
Discussion: The accessibility of the virtual format was suited to the population. Experiential activities were successfully adapted for online delivery. Managing seizure risk virtually was challenging and was mediated by the consideration of an appropriate platform. The reach and communication of group advertisement to appropriate referrers was challenging during busy service periods, to ensure sufficient referrals to make the sessions viable.
Conclusion: Moving forward the service will be widening access of the ACT group to referrals from other paediatric clinical health teams within Gwent (July 2021). We will continue with interprofessional delivery to promote psychological working across disciplines and wider dissemination of psychological resource. More formal and systematic appraisal of group efficacy will be key for future development.

Poster 078

Could pyridoxine supplements be used to ameliorate behavioural and neuropsychiatric side effects of epileptic children on levetiracetam? A local experience from a case series of epilepsy patients at Luton and Dunstable University Hospital UK

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Objective: Levetiracetam is one of the most common anti-epileptic drugs (AEDs) prescribed across all age groups due to its proved efficacy against multiple types of seizures, in addition to its tolerability, safety, and quick titration. However, various neuropsychiatric adverse events (NPAEs) have been reported with its use that could necessitate early discontinuation of the drug. Based on previous published literature that suggests possible efficacy of pyridoxine supplements in controlling levetiracetam related NPAEs, we are presenting a case series of 6 patients who have been commenced on pyridoxine in a trial to relieve levetiracetam related NPAEs instead of stopping the drug.
Methods: We have retrospectively analyzed electronic clinical records of 6 epilepsy patients who have been initiated on pyridoxine, when NPAEs have been reported on levetiracetam, as a case cohort of paediatric epilepsy patients at a district general hospital. Reported NPAEs related to levetiracetam were mood swings, hyperactivity, disturbed sleep and aggressiveness with a dose ranging from (25–38mg/kg/d). We gathered results of subjective feedback from parents about response in their behavior, 2–3 weeks after starting pyridoxine supplements with a dose ranging from (25–100mg/d).
Results: All of the 6 patients have positively responded with improvement in these behavioral symptoms after commencing of pyridoxine supplements. One of them did not improve with the lower dose of 50mg/d, but then started to show improvement on a higher dose of 100mg/d. There were no treatment related side effects from pyridoxine.
Conclusions: Pyridoxine supplementation has shown positive effect in most of our patients in improving the unwanted NPAE of levetiracetam, supporting findings of previous published reports. However, better evidence with high quality studies are required to explore the potential role of pyridoxine in management of NPAE related to different AEDs.

Poster 079

Unusual cause of treatable acquired communication deficit in childhood with excellent outcome in two patients

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Case Report: We present two unrelated children, a six-year-old female, and a 10-year-old male from different families; previously healthy, born at term with no adverse birth events and had normal development. The female presented with history of regression of expressive followed by receptive language, dropping school performance and memory difficulties. She then had generalised clonic and absence seizures. The male a had regression in behaviour, language and reading, difficulty in co-ordinating motor tasks and word finding followed by prolonged focal seizures which were sometimes secondarily bilateralised. Neurological examination was normal except for verbal auditory agnosia in both. EEG showed infrequent spikes over temporal regions in wakefulness, which became bilateral and very frequent in slow wave sleep consistent with diagnosis of focal electrical status epilepticus in sleep (ESES) of Landau-Kleffner syndrome (LKS) subtype. Basic blood tests, genetic tests, chromosomal microarray and epilepsy genetic panel to look for GRIN2A were negative. The clinical features of decline in language function and electrographic features confirmed the diagnosis of ESES seen in LKS. They received pulse dose methylprednisolone followed by tapering doses of oral prednisolone and remained on anti-epileptic medications. This resulted in significant speech and behaviour improvement as well as near complete remission of spike wave discharges in slow wave sleep.
Discussion: Landau-Kleffner syndrome (LKS) is a very rare epilepsy syndrome of childhood. Its main features are a loss of speech and language skills, seizures, learning and behaviour problems. It is a treatable cause of acquired communication deficit and

presents at a later age than autism and requires a high index of clinical suspicion. Although, the awake EEG may appear essentially normal, it is the sleep changes that clinch the diagnosis, therefore an overnight sleep EEG that aims to capture full sleep cycle, mainly slow wave sleep is crucial.

Poster 080

The use of Ataluren in a patient with CDKL5 deficiency disorder caused by a nonsense variant

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Background: Cyclin-dependent kinase-like 5 deficiency disorder (CDD) is a cause of early-onset epileptic encephalopathy characterised by seizures, global developmental delay and generalised hypotonia. Associated epileptic seizures are frequently refractory to treatment and there is no current targeted therapeutic option, although therapeutic options, such as the drugs Ganaxalone and Ataluren are under review in phase 3 and 2 trials respectively. There are 317 reported pathogenic variants of the CDKL5 gene of which 11% are nonsense variants. Ataluren is a novel small read through molecule compound that targets pathogenic nonsense variants.
Case Discussion: Here, we describe a case of a female with CDD caused by a de novo nonsense variant. She presented at 12 weeks with generalised tonic-clonic seizures during sleep. It was noted that she had central hypotonia and global developmental delay. Her seizures were difficult to control, despite trials of multiple high dose anti-seizure medications, vagus nerve stimulator and ketogenic diet. Ataluren was prescribed, on compassionate grounds, when she was 14 years old. It has been well tolerated over a two-year time period. Though no reduction in seizure frequency her family and assessments from the wider multidisciplinary team of neurologists, teachers, and physiotherapists, have reported improvements in behaviour and motor function. These functional improvements suggest that for the subset of patients with CDD with nonsense variants, there may be a role for Ataluren, though, further studies are needed to confirm this.

Poster 081

A case of KCNQ2 epilepsy presenting with intractable seizures, responding to sodium channel blockers and crucially dependent on drug levels

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Objective: To illustrate the clinical presentation of a neonate with intractable seizures who failed to respond to conventional anticonvulsant therapy. Sodium channel blockers were introduced following his genetic diagnosis and were effective but only at high serum levels.
Methods: This is a case report of a male neonate presenting with an epileptic encephalopathy on day 4 of life. He was a term baby born in good condition following an unremarkable pregnancy. There was a family history of epilepsy in more than one generation. Seizures were daily and took many different forms, either clusters of short focal seizures between 1–5 minutes or he had secondarily generalisation with status epilepticus. Despite multiple standard anticonvulsant medications which included Phenobarbitone, Levetiracetam, Midazolam and Zonisamide at appropriate doses. His seizures remained intractable leading to a prolonged inpatient stay of 60 days. Detailed biochemical and metabolic investigations were normal. MRI brain showed non-specific white matter changes. Electroencephalography supported a multifocal epilepsy.
Results: Trio exome sequencing confirmed the diagnosis of KCNQ2 epilepsy. Once the genetic diagnosis was made, Sodium channel blockers were introduced. He became seizure free but notably only when there were high and stable levels of Phenytoin and subsequently of Carbamazepine.
Indeed Phenytoin levels needed to run between 15 and 19mg/l (Normal range 10–20mg/l) and Carbamazepine levels more than 6mg/l (normal range 4–7mg/l) at all times to maintain seizure freedom. This was observed throughout the 11-month period of follow up.
Conclusion: It is recognised that KCNQ2 neonatal epileptic encephalopathy responds to sodium channel blockers. Our case illustrated that high drug level of these medications can be crucial to control the seizures.

Poster 082

Delphi consensus for the UK guideline for management and surveillance of idiopathic intracranial hypertension (IIH) in children and young people

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Background: We conducted a national Delphi consensus process to inform a national guideline for the management of IIH in children and young people in the UK. There is no strong evidence to support the way IIH is diagnosed or treated so it is important we gain consensus where possible and identify important areas of uncertainty and variation in practice.
Methods: The Delphi focused on all aspects of IIH including initial assessments (referral criteria, clinical assessments, laboratory tests, lumbar puncture, ophthalmology assessments and investigations, and imaging), diagnosis (diagnostic criteria and terminology) and treatment options (including conservative, drug and neurosurgical interventions), follow-up, and surveillance. General paediatricians, paediatric neurologists, ophthalmologists, opticians, neuroradiologists, and neurosurgeons known to have a clinical interest or experience in IIH were invited to take part. The questions were designed by a core committee representing all relevant disciplines. The charity IIH-UK contributed to represent patients and their families. A priori consensus was defined as 70% agreement.
Results: This project started in March 2019 and was completed in August 2021. The Delphi consisted of three rounds with 104 questions. There were 54 and 66 responders for the first two rounds. The Delphi was endorsed by the Royal College of Ophthalmologists

which engaged 59 ophthalmologists for round three. Key areas in which there was a high consensus included: Baseline blood tests; How lumbar puncture is performed and CSF pressure recorded; Diagnostic criteria; Ophthalmology assessments; Brain and ophthalmology imaging; Treatment options including LP, medical and surgical treatment; Follow up and surveillance.
Conclusions: This new UK consensus for the management and surveillance of IIH provides a realistic and pragmatic approach, based on expert opinion for best clinical care for children and young people with IIH. We hope these recommendations will minimise under and over diagnosis, improve the care offered, and outcomes obtained.

Poster 083

Greater occipital nerve block in the management of refractory headache in children

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Objective: To study the tolerability and efficacy of Greater Occipital Nerve Block (GONB) in the management of children with refractory headache.
Methods: This a retrospective service evaluation study of the use of GONB in the treatment of children with headache over the past 3 year. Data were collected on children's demography, clinical characteristics, GONB procedure, adverse effects and response to treatment. Good response was defined as freedom of headache for ≥2 weeks after injection, partial response, as freedom of headache for <2 weeks or reduction of pain intensity that allows the child to participate in normal activities and no response is defined as lack of improvement.
Results: Fifty children were treated over a 3 year-period; 36 (72%) were female and mean age was 14y (range: 11–17). Twenty-nine (58%) children have Chronic Migraine, 8 children have frequent Episodic Migraine, 3 have Episodic Migraine and Chronic Tension Type Headache, 2 children have Hemicrania continua, 2 have Persistent Post-traumatic Headache and 6 children have mixed headaches. All children had previously failed up to 5 standard prophylactic medications; an average of 3. All children except 2 tolerated the procedure well. A total of 77 treatment sessions were given (average 1.6 session per child; range 1–3). Bilateral injections were given on 37 occasions and unilateral on 40. Complete data were available on 73 treatment session; 46 (63%) resulted in good or partial response and 27 (37%) had no response.
Conclusions: GONB has a role to play in the treatment of children with difficult to treat headache. Controlled trials are needed to validate the results of this observational study.

Poster 084

Tertiary neurology experience of secondary pseudo tumour cerebri presenting with headache in children

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Objectives: To identify the varying secondary causes of pseudo tumour cerebri, so as to ensure timely management and to avoid the diagnostic delays.
Methods: A retrospective case note review of children aged 5 to 16 years was conducted in a tertiary neurology centre, between 2018 to 2020. The ICDH-3 criteria were used to diagnose PTCS. The age, sex, symptoms, fundoscopic examination, CSF pressure, cranial MRI, MR venography and treatment of each patient were noted.
Results: Definition of secondary PTCS excludes abnormal brain parenchyma, infection, and tumours. Out of 40 children presenting with headache, 31 (77.5%) were diagnosed with Idiopathic Intracranial Hypertension. Rest 9 (22.5%) children were found to have underlying pathologies. 8 out of the 9 (88.8%) children were female. The mean age at presentation was 11 years. Presenting complaints were headache (66.6%, n=6), asymptomatic disc oedema (22.2%, n=2), right-sided numbness and reduced concentration (11.1%, n=1 each). Headache phenotype is described as severe intensity pain all over the head or in frontal and occipital region, episodes ranging from few times a week to daily with associated nausea, vomiting and blurred vision. All these patients had similar signs and symptoms as compared to the patients with confirmed IIH. Of these 9 children, 3 were found to have underlying causes attributed to craniopharyngioma, Chiari malformation, and Anti-NMDA encephalitis, hence were excluded from secondary causes. The remaining 6 patients were identified to have secondary causes such as CVST, obesity, steroid use, craniosynostosis and hypothyroidism. They were treated with acetazolamide, topiramate and medications for underlying pathology, with resolution of symptoms and none required surgery.
Conclusion: Pseudotumor cerebri can cause irreversible vision loss. Morbidity associated with visual loss, pain and reduced quality of life warrants accurate identification, evaluation and treatment of children with secondary PTCS. A multidisciplinary team management is essential for this elusive and life-limiting condition.

Poster 085

An audit of paediatric headache referrals and management in the outpatient clinic in Doncaster Royal Infirmary

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Background: Headaches have significant impact on the children and young adults health and quality of life. Recently there has been an increasing number of children who are referred to Doncaster Royal Infirmary with a primary problem of headache. Therefore, there was an urgent need to evaluate whether our current practice is in the accordance of existing NICE guidelines on headache and best practice, and to provide solutions for the shortcomings in some aspects of the service.
Standards: NICE Standards: CG150 and NG127: (1) People with tension-type headache or migraine are not referred for imaging if they do not have signs or symptoms of secondary headache. (2) Using a headache diary to aid the diagnosis of primary headaches.
Methodology: Data collected by looking at Dr Habib clinic HS21N for patients diagnosed with Headache – then looked at casenotes and Medisec system for data. All children under 16 years old who were diagnosed with headache during the period of January 2019 to December 2020 were included and those whose headaches were not the primary reason for referral were excluded. After application of inclusion and exclusion criteria, 51 patients were included in the audit.

Results: 60% of patients were female and GP was the commonest route of referral (82%). Only 2 patients had kept a standardised headache diary when attending the 1st clinic. Blood pressure was performed for all patients who were seen face-to-face. The neuroimaging was performed on only 1 patient in the clinic and on 2 patients before referral to the clinic. 41% of patients reported improvement in their headaches in the second clinic visit.

Recommendations and action plan: (1) Develop Headache referral pathway. (2) Print, disseminate and communicate to the GPs and junior doctors the need to use the diary headache while patients are awaiting their appointment in the clinic.

Poster 086

Hemiplegic migraine presenting as a stroke mimic

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A 15-year-old teenager, presenting with left-sided headache and a behavioural change with dysarthria and dysphasia. His neurological examination showed right sided facial weakness that resolved after a couple of hours. He also was agitated and developed apneas needing intubation and ventilation. All scans including MRI and MRA were reported as normal. Susceptibility-weighted imaging (SWI) sequences demonstrated vascular asymmetry and was most helpful in providing diagnostic information. He was back to normal after 24 hours. A repeat MRI brain 2 months later showed similar vascular filling bilaterally. He remained well at follow up and his neurological examination remained normal. Hemiplegic migraine either occurs sporadically or is familial. It presents with headache and motor weakness which may be associated with visual or sensory manifestations, speech impairment or brainstem aura. Motor symptoms last <72 hours. MR sequences that are most helpful are SWI sequences and Diffusion weighted imaging (DWI). SWI and DWI are fast sequences and can demonstrate early tissue ischemia or haemorrhage in time critical diagnoses. There is reported asymmetry in the cerebral vessels between both brain hemispheres depending on the imaging timing and showing either hypoperfusion or hyper perfusion. This is called the BOLD effect. Paediatricians should be aware of the utility of MRI SWI sequences, which are readily available and can be rapidly performed for time critical diagnoses.

Poster 087

Probabilistic targeting for paediatric deep brain stimulation: 'Hot Spot' or 'Pot Shot'?

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Objectives: Variation in outcomes following Deep Brain Stimulation (DBS) surgery likely in part to relate to differences in electrode location between patients. In adult patients with dystonia Probabilistic Stimulation Mapping (PSM) techniques have suggested a 'hot spot' within the GPi correlating with better outcome. We aimed to determine for a cohort of children and young people (CAYP) undergoing DBS targeting the Globus Pallidus Interna (GPi) bilaterally whether a similar 'hot spot' could be found.

Methods: A retrospective analysis of 31 CAYP with genetic or idiopathic dystonia and 22 CAYP with Cerebral Palsy was performed. Post-operative CT images were linearly registered to pre-operative MRI sequences, followed by non-linear normalisation to the MNI space. All 106 implanted electrodes were automatically reconstructed, and Volumes of Tissue Activations (VTAs) were generated based on individualised patient programming. Left sided VTAs were non-linearly flipped to the right. For the Genetic dystonia group, voxels in each VTA were labelled by improvement in BFMDRS score at one year post surgery. PSMs were generated based on the average improvement at each voxel. For the CP group, COPM scores were used as the main outcome measure.

Results: In the genetic dystonia group, improvement in BMFDRS was seen with electrodes across a broad area of insertion. Thresholding the PSM to voxels in the 75th Centile or above of average response identified a discrete cluster (hot spot) slightly more posterior and superior than the typical GPi target (Centre of Gravity MNI coordinates X= 23.0, Y= -9.7 and Z= -3.8). For the CP group, better COPM outcomes were associated with voxels in a less distinct volume anterior to this target.

Conclusion: PSM demonstrated an apparent 'hot spot' for CAYP with genetic dystonia, informing future targeting strategies. Group wise targeting strategies for CAYP with CP may not be valid.

Poster 087a

[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.]

Paroxysmal movements in 2 children

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Poster 088

Cognitive strategies and underlying mechanisms in childhood-onset hyperkinetic movement disorders including dystonia

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Background: There is a significant gap in knowledge about rehabilitation techniques and strategies that can help children and young people with hyperkinetic movement disorders (HMD) including dystonia to successfully perform daily activities and improve

overall participation. A promising approach to support skill acquisition is the Cognitive Orientation to daily Occupational Performance (CO-OP) intervention. CO-OP uses cognitive strategies to help patients generate their own solutions to overcome self-identified problems encountered in everyday living.
Objectives: (1) To identify and categorize strategies used by children with HMD to support skill acquisition during CO-OP; (2) To review the possible underlying mechanisms that might contribute to the cognitive strategies, in order to facilitate further studies for developing focused rehabilitation approaches.
Methods: A secondary analysis was performed on video-recorded data from a previous study exploring the efficacy of CO-OP for childhood onset HMD, in which CO-OP therapy sessions were delivered by a single occupational therapist. For the purpose of this study, we reviewed a total of 40 randomly selected hours of video footage of CO-OP sessions delivered to six participants (age 6–19 years) over ten intervention sessions. An observational recording sheet was applied to identify systematically the participants' or therapist's verbalizations of cognitive strategies during the therapy. The strategies were classified into seven categories in line with published literature.
Results: Strategies used by HMD participants included distraction, externally focussed attention, internally focussed attention, self-regulation, motor imagery, mental self-guidance and stabilisation. We postulate different underlying working mechanisms for these strategies, which have implications for the therapeutic management of children and young people with HMD including dystonia.
Conclusions: Cognitive strategy training can fundamentally change and improve motor performance. On-going work will address both the underlying neural mechanisms of therapeutic change and the mediators and moderators that influence how change unfolds.

Poster 089

Intrathecal Baclofen pump test dosing- what is current UK and Ireland practice?

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Objective: To establish current practice in Intrathecal Baclofen (ITB) test dosing in the UK and Ireland. To find out what perceived value of test dosing was to centres who deliver it.
Methods: An electronic survey was sent out to all centres in the UK and Ireland who currently carry out ITB pump insertion. A reply was received from every centre.
Results: Majority of centres conduct ITB test doses prior to insertion of ITB pumps. A minority of centres will proceed directly to ITB pump implantation without test dose in certain situations (palliative and urgent cases). Methods of administering test doses include spinal catheters with manual boluses or infusion pumps and lumbar puncture injection. 80% of centres would not proceed to pump insertions if test dose had no positive effects. 50% would implant an ITB pump even if there had been an adverse response to test dosing (although the need for a careful discussion of risks vs benefits was highlighted). Most centres agree that test dosing is useful to the clinical team; and strongly agree it is useful to families. All centres had some delays to their test dosing due to the COVID-19 pandemic in 2020 from <3 months to not taking place at all.
Conclusions: A consensus on UK and Ireland practice for ITB test dosing needs to be developed. Practice is not uniform across the centres surveyed. However, the majority feel test dosing is of benefit to clinical teams and the family of the child or young person involved.
Acknowledgements: With thanks to survey respondents from Leeds Children's Hospital, The Evelina Children's Hospital, Sheffield Children's Hospital, Southampton Hospital, Alder Hey, Temple Street Hospital (Dublin), Ninewells Hospital (Dundee), Royal Hospital for Sick Children (Edinburgh), Great North Children's Hospital, Queens Medical Centre (Nottingham), Tayside Children's Hospital, John Radcliffe Hospital (Oxford).

Poster 090

Homozygous mutation in mitochondrial Cysteinyl-tRNA synthase gene (CARS2) presenting as movement disorder, developmental regression and epilepsy

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Mitochondrial disorders are suspected in children with developmental regression with epilepsy. Newer genetic approaches with trio exome and whole genome sequencing are enabling clinicians detecting rarer genetic conditions in consanguineous population in UK. We present a rare case of CARS2 gene homozygous mutation.
Case Report: A 6 year old male of Pakistani descent referred to hospital with worsening recurrent falls with onset at 4 years. Male was 1st born of consanguineous parents related as cousins, has uneventful pregnancy and birth. Initial development was normal except mild delay in motor milestones. Tremors and myoclonic jerks resulted in recurrent falls leading to injuries particularly when tired. At 6 years of age he presented with generalised tonic clonic seizures in sleep at monthly intervals and also reported absences. Clinical examination showed few café-au-lait patches, normal physical growth, truncal and peripheral tremor at rest and in action, cerebellar signs and nystagmus. Initial metabolic blood results including white cell enzymes, genetic array CGH and neuroimaging were normal. An awake interictal electroencephalogram showed multifocal epileptiform spike and slow waves bilaterally. A joint neurogenetic clinical review recognised progressive degenerative condition, hence a rapid trio-exome sequence analysis was ordered which revealed homozygous CARS2 splicing variant (NM_024537.4:c.655G>A). Both parents were identified as carriers. Epilepsy was managed with Levetiracetam resulting in remission of motor seizures. Multidisciplinary management and education support were put in place.
Discussion and Conclusion: There are few reported cases of CARS2 related mitochondrial disorder in the medical literature. The presentation with developmental delay, epilepsy and movement disorder are consistent with previous cases but additionally we report neuroregression in our proband. The widespread availability of trio exome and whole genome sequencing will identify further affected individuals and increase the knowledge of this rare condition.

Poster 091

Attitudes towards the neurological examination in an unwell term neonate: a mixed methods approach

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Objective: To review confidence of UK paediatricians in the neurological examination of an unwell term neonate and determine attitudes towards it.
Methods: An explanatory sequential mixed methods approach (QUAN→QUAL) with equal weighting between stages from UK paediatric and neonatal units. Paediatric clinicians completed a survey, including free text boxes and Likert scales. The last question asked for volunteers for a qualitative descriptive study involving semi-structured interviews. A snowball technique identified additional participants. Thematic analysis was used to interpret qualitative data, which was triangulated with quantitative questionnaire data.
Results: 193 surveys from at least 60 UK paediatric units were obtained. 31.0% worked in neonatology, 59.7% in paediatrics, 9.3% in paediatric neurology. 47.7% were consultants. The median range for confidence was 4 (IQR3–5). Senior responders scored higher confidence than trainees. High-quality documentation of the neurological examination was reported in half of unwell term neonates. Thematic analysis revealed three themes, which we will discuss in detail: 'Current culture on neonatal units', 'Changing the culture', and 'Practicalities of the neurological examination in unwell term neonates'. Most interviewees had not been trained in the neonatal neurological examination, did not know how to perform or interpret it, described it as low value, and made excuses to avoid it. Undue emphasis was placed on other investigations, such as imaging or neurophysiology.
Conclusions: Although survey responders reported confidence in the neonatal neurological examination, clinicians told us they did not know how to perform it and reached a state of confidence by assuming they were doing it right. Additional emphasis was put on other investigations, and teaching trainees rarely occurred. A simple, standardised neurological examination with dedicated training would improve this culture.

Poster 092

Evaluating a neonatal coma score in preterm and sick term neonates

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Background: There is no accepted neonatal coma score (NCS). We previously devised a NCS and validated it in term neonates. A normal score was 13–15 out of 15. This study evaluated the use of the NCS in preterm and unwell, term neonates and looked for evidence it could identify neonates who deteriorated neurologically.
Methods: Preterm and term neonates were recruited. Nurses performed the NCS every six hours for the duration of their admission until discharge. We explored the relationship between NCS and corrected gestational age (CGA) using ANCOVA to estimate the correlation coefficient. Medical and nursing records of neonates who demonstrated significant variation in NCS were reviewed and possible causes determined.
Results: 50 neonates were recruited. The median corrected gestational age at time of consent was 33+2 weeks (range: 24+4 – 41+6). 42 neonates were premature. In premature participants, there was a significant correlation between NCS and corrected gestation age (correlation coefficient 0.55, $p<0.05$). Most premature infants >35wks CGA had a normal score >13. Significant variation in the NCS was observed in 10 preterm neonates and 1 term neonate. Drops in NCS were related to sedation and paralysis, sepsis, suspected necrotising enterocolitis, neurosurgery, retinopathy of prematurity screening, and cerebrospinal fluid taps in some neonates with hydrocephalus.
Conclusion: The NCS provides clinically useful information. The NCS changes with CGA and a normal score is reached by around 35 weeks. Our data suggests the NCS detects deterioration in conscious levels related to illness, drugs and surgery. We struggled to recruit term babies and a deferred consent method would be more appropriate for future work. Results from a larger cohort are needed to confirm its clinical utility, how it is related to amplitude integrated electrocephalopathy, and whether it has value in assessing term babies with hypoxic ischaemic encephalopathy for hypothermia treatment and in prognostication.

Poster 093

Cerebral infarcts secondary to neonatal polycythaemia

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Introduction: A rare case of a newborn baby with cerebral infarcts as a result of Polycythaemia.
Case description: A case of a three-day-old baby presented to the emergency department with right side focal seizures. It recurred 3 times in a short period and therefore needed a loading dose of IV phenobarbitone. Precipitous birth history with an unplanned home delivery, resulting in delayed cord clamping and low held baby. The birth weight was only 2.465 kg (9th centile). Normal full septic, metabolic and thrombophilia screen. Echocardiogram was normal. Cranial USS and MRI scan findings were suggestive of multiple deep infarcts. EEG was abnormal. His haemoglobin was high (247 g/l) with high haematocrit (0.67), which responded quickly to fluid bolus followed by nasogastric feeds. He was treated with antibiotics and aciclovir for possible CNS sepsis, subsequently stopped following the negative cultures and PCR. Over the following outpatient assessments, no further seizures with normal neurological and developmental evaluation.
Discussion: Neonatal Polycythaemia, defined as the haematocrit and haemoglobin are >0.65 and >220 g/L respectively from venous sampling, occurs in approximately 1–5% of newborn babies. Both delayed cord-clamping and IUGR played a role in our baby's Polycythaemia. Polycythaemia can lead to hyperviscosity of the blood, which is responsible for some of the symptoms. In neonates, there is an exponential relationship between haematocrit >0.65 and blood hyperviscosity is a slight increase in haematocrit results in a significant increase in viscosity. Over 74% of neonates with Polycythaemia are asymptomatic. Brain infarcts are extremely rare complications of neonatal Polycythaemia. For neonates with a haematocrit >0.65 and symptoms that may be

precipitated by hyperviscosity, the most common management method is IV hydration and observation. However, as in our case, enteral hydration can also be very effective with excellent long-term outcomes.

Poster 094

COL4A1 mutation: Don't miss the antenatal clues!

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Objectives: The COL4A1 (Collagen type IV alpha 1) gene encoding the type IV collagen alpha 1 chain is an essential component of the basal membrane stability. The neurological manifestations of this potentially multi-system disease are well described including porencephaly, cortical malformations and small vessel disease. We report preterm twins who were diagnosed with COL4A1 gene-associated cerebral disease following surveillance antenatal ultrasound scanning demonstrating evolving intracranial haemorrhage and porencephaly.
Methods: A fit and well mother underwent regular antenatal surveillance imaging during her second pregnancy with twins, as her first pregnancy was terminated at 36 weeks following antenatal scans revealing intraparenchymal haemorrhage and cysts. A post-mortem MRI at 37 weeks confirmed a large porencephalic cyst. The antenatal scans for the twins demonstrated progressive intracranial haemorrhage from 20 weeks gestation evolving into cysts by 28 weeks gestation. They were born prematurely at 31 weeks gestation when she went into spontaneous labour.
Results: Although prematurity is associated with intraventicular haemorrhages and subsequent porencephalic cyst formation, this is usually triggered off by the process of labour, which affects the fragility of preterm brain vasculature. In this case, the preceding antenatal evolution of intracranial events warranted further consideration. Genetic testing confirmed a pathogenic heterozygous mutation in COL4A1 in both twins.
Conclusions: COL4A1 mutations are most frequently tested in term infants who are born with porencephalic cysts. We highlight the importance of testing for this in infants of all gestations who present with unexplained spontaneous antenatal intracranial haemorrhage or porencephaly.

Poster 095

Caudal Regression Syndrome type III following gestational diabetes (in a Sri Lankan setting)

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Introduction: Caudal Regression Syndrome is a rare congenital anomaly which has an incidence of approximately 1 per 100,000 new-borns and severe variants are often associated with cardiovascular, pulmonary, gastrointestinal, and musculoskeletal abnormalities. We report a two-month old child in whom the diagnosis of caudal regression syndrome type III was confirmed based on clinical and radiological characteristics.
Case Report: A two-month-old child presented for evaluation of multiple congenital abnormalities. He had two healthy older siblings. Antenatal period was uncomplicated apart gestational diabetes which was not controlled during the second trimester and before the diagnosis was made. He had been having urinary and faecal incontinence since birth. Growth was age appropriate. Physical examination revealed a narrow pelvis, bilateral knee flexion contractures, bilateral leg muscle atrophy, and bilateral congenital talipes equinovarus deformity with diminished ankle joint creases. He had clinical evidence bilateral hip dysplasia with positive Ortolani's and Barlow's test. Other abnormalities included micropenis (stretched penile length – 1 cm), displaced patulous anus with tiny pressure sores and flat, dimpled buttocks (Patient photographs available). Ultrasound revealed complete agenesis of the sacrum and L5 vertebra. The iliac bones were articulated with L4 vertebral body. The cord had terminated abruptly at L1 level. Thickened conus medullaris was seen. There was no evidence of either meningomyelocele or meningocele. Ultrasound of hips revealed bilateral hip dysplasia with shallow acetabula. Overall, the findings were in keeping with type III caudal regression syndrome. Ultrasound abdomen showed no evidence of renal agenesis, neuropathic bladder, vesico-ureteric reflux, or bowel malrotation. Parents were counselled regarding long term prognosis and available supportive treatment options. Long-term follow up was arranged with general paediatrician, paediatric neurologist, and orthopaedic surgeon.
Conclusion: Poorly controlled/undiagnosed gestational diabetes is not an uncommon scenario in a Sri Lankan setting. This report highlights importance of optimal control of antenatal blood sugars to prevent several future complications including sacral agenesis in the new-born.

Poster 096

Safety of IncobotulinumtoxinA in multipattern treatment of upper and lower limb spasticity in children/adolescents with cerebral palsy: pooled analysis of 3 large phase 3 studies

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Introduction: This analysis assessed the safety and tolerability of repeated incobotulinumtoxinA treatment for lower-limb (LL), upper-limb (UL), or combined LL/UL spasticity in ambulant and non-ambulant children/adolescents with cerebral palsy (CP) using pooled data from 3 large Phase 3 studies.
Methods: Pediatric patients with spasticity (2–17 years of age; uni- or bilateral CP; Gross Motor Function Classification System [GMFCS] level I-V; Ashworth Scale [AS] score ≥2 in clinical patterns for treatment; clinical need for treatment) were enrolled.

Patients received total body incobotulinumtoxinA doses of 16 U/kg body weight (BW, ≤400 U) for LL spasticity in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL/UL treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Adverse events (AEs) were assessed in the pooled population.
Results: In total, 907 patients (59.6% male, mean [SD] age 6.7 [4.2] years, BW 23.3 [13.9] kg) received multipattern treatment; 753 patients (83.0%) completed the studies and received up to 6 ICs. Across all ICs, 363 (40.0%) experienced an AE; 33 (3.6%) had ≥1 treatment-related AE. The most common AEs were nasopharyngitis, bronchitis, and upper-respiratory tract infection. Serious AEs (SAEs) and AEs of special interest (AESIs) were reported for 49 (5.4%) and 18 (2.0%) patients, respectively. AESIs reported in >1 patient were muscular weakness (6 patients, 0.7%), dyspnea, constipation, and dysphagia (3 patients, 0.3% each). There was no increased incidence of AEs, SAEs, or AESIs with repeated dose. No deaths were reported in these studies.
Conclusions: IncobotulinumtoxinA was safe and well tolerated for LL, UL, or combined multipattern treatment over up to 6 ICs in a comprehensive population of ambulant and non-ambulant pediatric patients with spasticity (GMFCS levels I-V).

Poster 097
Improvement of spasticity-related pain with Incobotulinumtoxina treatment in children/adolescents with cerebral palsy: pooled analysis of 3 phase 3 studies

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Introduction: Spasticity-related pain (SRP) in children and adolescents with cerebral palsy (CP) is common, often neglected, and impacts daily quality of life. We assessed the effect of incobotulinumtoxinA on SRP using pooled data from 3 large Phase 3 pediatric studies.
Methods: Ambulant and non-ambulant patients (2–17 years of age; uni- or bilateral CP; Ashworth Scale score ≥2 in clinical patterns for treatment) were enrolled. Patients received total body incobotulinumtoxinA doses of ≤16 U/kg (≤400 U) for lower-limb (LL) treatment in 2 injection cycles (ICs) in TIM (NCT01893411). In TIMO (NCT01905683), TIM completers and new recruits received 4 ICs with 16–20 U/kg (≤400–500 U) for LL or combined LL and upper-limb (UL) treatment. In XARA (NCT02002884), patients received 4 ICs with 16–20 U/kg (≤400–500 U) for UL or combined LL/UL treatment. Changes in self-reported (child/adolescent) or observed (parent/caregiver) SRP were assessed using the Questionnaire on Pain caused by Spasticity (QPS) in patients with LL (TIM, TIMO, and XARA) and UL treatment (TIMO and XARA).
Results: Assessments for 849 patients with LL and 454 patients with UL treatment were included. Of these, 340 (40.0%, LL: 61.2% male, mean [SD] age 9.3 [3.8], body weight [BW] 32.6 [14.8] kg) and 160 (35.2%, UL: (61.9% male, mean [SD] age 10.3 [3.7] years, BW 36.8 [16.5] kg) were able to assess SRP by interviewer- or self-administered QPS. Most (81.9% LL; 69.7% UL) reported pain at baseline for ≥1 activity. SRP increased with activity demands. Complete SRP relief at Week 4 post-treatment in each IC was seen (Table) and was highest in IC4. Observed SRP frequency was consistent with self-reported SRP and was supported by respective QPS item scores (all P<0.001 for responder rates).
Conclusions: In this large, pooled analysis, repeated incobotulinumtoxinA injections led to sustained pain reduction in children and adolescents with spasticity, with complete pain relief in the injected limb during activities in ≤54.8% of patients.

Poster 098
Common features in children with known genetic cause for cerebral palsy.

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Background: Cerebral palsy (CP) has a complex aetiology with several contributing factors such as prematurity, infection and hypoxic-ischaemic injury which are well understood and have guided clinical treatment and prevention, reducing prevalence. There is an emerging understanding of the genetics behind this complex disorder with Increasing knowledge of both genetic susceptibility genes, copy number variants and rarer monogenic mutations, which can drive research towards targets for intervention and precision medicine.

Objectives: To characterise the clinical presentation of children with an underlying genetic cause for their cerebral palsy and to identify common features possibly predictive of underlying genetic abnormality.
Methods: From a cohort of 221 patients in Cambridgeshire aged 0–18 years who all had a clinical presentation consistent with CP, we identified 11 cases with a genetic diagnosis identified. We analysed their clinical records to identify common themes likely from literature to be atypical.
Results: Of 9 patients, 4 were male (36.3%) and 7 were female (63.6%). Identified features more likely to be seen in genetic CP included: normal gestation and delivery, epilepsy type or severe intellectual disability out of keeping with presentation, congenital abnormalities, dysmorphic features, atypical MRI findings and a family history. 9/11 (81.8%) patients had at least 4 of the 7 features we have identified in total and 6/11 (54.5%) patients had at least 5 out of the 7 features we have identified in total. The most common features included: unexpected severe intellectual disability (9/11 patients), normal gestation and delivery (8/11 patients), dysmorphic features (9/11 patients) and atypical MRI findings (9/11 patients).
Conclusions: In patients with a genetic underlying cause identified for their cerebral palsy, there are a number of common features

identifiable from clinical history and presentation. These factors could be useful in clinical practice as we consider genetic testing more widely in children.

Poster 099

Pooled efficacy analysis of Incobotulinumtoxina in the multipattern treatment of upper- and lower-limb spasticity in children and adolescents with cerebral palsy

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Introduction: This pooled analysis assessed the efficacy of incobotulinumtoxinA for lower-limb (LL) and upper-limb (UL) spasticity in children and adolescents with cerebral palsy (CP) using data from the first controlled injection cycle of 2 large Phase 3 studies, TIM (NCT01893411) and XARA (NCT02002884).
Methods: Ambulant and non-ambulant pediatric patients with spasticity due to CP (2–17 years of age; uni- or bilateral CP; Ashworth Scale [AS] score ≥2 in clinical patterns for treatment) were enrolled. Patients were randomized (2:1:1) to 3 incobotulinumtoxinA dose groups: 8, 6, 2 U/kg body weight (BW), maximum 200, 150, 50 U per LL clinical pattern in TIM and per UL in XARA. Additional multipattern treatment was allowed in both studies with total body doses up to 16–20 U/kg BW (≤400–500 U) depending on study and Gross Motor Function Classification System (GMFCS) levels I-V. Changes from baseline in AS score and Global Impression of Change Scale (GICS) scores at Week 4 were assessed in patients with LL treatment (TIM and XARA) and in those with UL treatment (XARA).
Results: In total, 603 patients with LL treatment from both studies (58.9% male, mean [SD] age 6.8 [4.2] years, BW 23.6 [13.5] kg, 27.2% GMFCS IV-V) and 350 patients with UL treatment from XARA (62.9% male, mean [SD] age 7.3 [4.4] years, BW 25.0 [15.0] kg, 30.9% GMFCS IV-V) were included in this analysis. Improvements in AS score for the main LL and UL clinical patterns were seen with all incobotulinumtoxinA doses at Week 4 (all $P<0.0001$ vs baseline except adducted thigh at 8 U/kg). Significantly greater improvement in AS score for the main UL clinical pattern was noted in the 8 U/kg versus the 2 U/kg dose group ($P=0.004$). Investigator's, child/adolescent's and parent/caregiver's GICS scores confirmed improvement in LL and UL spasticity at Week 4.
Conclusions: IncobotulinumtoxinA provides effective multipattern treatment of LL and UL spasticity in pediatric patients with CP (GMFCS I-V).

Poster 100

Dystonia in children with acquired brain injury

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Objectives: (1) To estimate the incidence/frequency of dystonia and/or status dystonicus after acquired brain injury (ABI) admitted to paediatric intensive care unit. (2) To analyse the trajectory of dystonia over a 6-month period.
Methods: The Children's Health Ireland at Temple Street PICU electronic database was searched for key terms related to ABI from January 2016 - March 2021. Individuals meeting inclusion criteria were further analysed and clinical data pertinent to dystonia, treatment and outcomes was recorded for analysis.
Results: Six-hundred and forty three PICU episodes (580 patients) met search criteria of key terms. Traumatic brain injury (TBI) was the most frequent ABI 109/580 (18.7%), followed by CNS infection 96/580 (16.6%). Twelve patients developed dystonia following ABI with an incidence of 2.1% overall and 6.4% in our TBI group. 3/12 (25%) developed status dystonicus. All patients developed dystonia within the first month following ABI (100%). All had evidence of severe injury (GCS 8 or less) at time of PICU admission and 3/12 (25%) required emergency neurosurgical intervention. Most commonly used medical therapy included clonidine (n=10), baclofen (n=10), gabapentin (n=5) and trihexyphenidyl (n=2). Often, requiring a combination of medications. Outcomes at follow up were variable. One patient died prior to 6-month follow up. Some patients displayed good functional improvements with rehabilitation, but most patients (8/11, 72.7%) continued to require medication for their dystonia 6 months after their injury.
Conclusions: The incidence of dystonia following ABI is 2.1% and 6.4 % in the TBI group. Dystonia typically emerges within a month of ABI and was persistent in the majority. Our patient cohort displayed variable outcomes, although sample size is small. We hypothesize that dystonia was under-recognised, and that the true number of patients who developed dystonia following ABI is greater than recorded.

Poster 101

Can we predict which children and young people with cerebral palsy and significant scoliosis will need operative vs non operative treatment?

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Can we answer the question: "Will my teenager with severe cerebral palsy need spinal surgery?" Paediatric disability literature describes the presence of scoliosis but rarely discusses its magnitude or whether surgical or non-surgical routes are offered. Orthopaedic papers tend group all causes of disability, mixing syndromic and cerebral palsy, despite their different natural histories. The decision to undergo surgery in this cohort, is often made remote from the paediatric teams known to the child in

earlier years. With access to a geographically based spinal deformity service for CYP with disabilities, we wondered if there was information to be able to help answer this question.
Methods: Retrospective notes review of all CYP attending spinal service born 1990 to 2000. CYP with significant scoliosis (Cobb over 50) and over 11 years (excludes early onset group) were identified. Active separation of cerebral palsy vs 'other ' syndromic / muscular / metabolic conditions.
Results: From 2010–2016, 80 CYP with severe scoliosis and complex disability were identified, of which 41 had cerebral palsy, creating a 'pure' diagnostic group. Of these 41 CYP, 22 have had spinal surgery, 19 did not. The decision not to have surgery was made as a positive choice between the surgeon the family and MDT, rather than due to medical vulnerability and surgical risk. Cobb angles were similar range and severity (surgical cohort 55 - 106, non-surgical 56 - 110) Decisions for management (surgery or non-surgical) ranged from 13 to 23 years of age. Mean age of surgery 16 (range 12 to 19).
Conclusion: Even in severe disability and scoliosis we found almost half were actively able to pursue conservative management – this is helpful for families and YP to know.

Poster 102
'Entry to exit' – neurorehabilitation journey for children with acquired brain injury: MDT perspective

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Objective: Neurorehabilitation is a long-term process for children with acquired brain injury (ABI). We sought to understand the perspective of multi-disciplinary team (MDT) members, their evaluation of current practice and their views on the development of a neurorehabilitation pathway underpinning the NHS England service contract for paediatric ABI.
Methods: A qualitative exploratory method that consisted of semi-structured interviews and a focus group discussion was used to analyse a patient's journey from admission to discharge from each profession's perspective. Data was collected from the consultant neurologist, the clinical psychologist, speech and language therapists, physiotherapists, occupational therapists, play specialists, hospital education service, nurses, dieticians, trauma coordinators, child brain injury trust coordinators, and the children with medical complexities team coordinator. Seventeen data-gathering sessions involving a total of 27 professionals were conducted in Birmingham Children's Hospital. Thematic analysis was used to analyse the data.
Results: The following six overarching themes and the associated sub-themes were developed: (1) Values (professional recognition, culture, and limited staff members). (2) Early help to families/ children. (3) Goal setting and MDT meeting. (4) Communication and behaviour (managing expectations, power balance and parent's concerns/emotions). (5) Barriers (housing, access to other services, and resources). (6) Effectiveness (joint working, outcome measures, benchmarking and supported discharge). The participants identified that whilst they were providing sufficient care for these children, there were deficiencies both at individual and team levels in the themes listed above, which needed addressing.
Conclusions: All the themes were interrelated and highlighted the need to consider them collectively to develop an integrated neurorehabilitation pathway. Although our findings are specific to the context in which the data were collected, the existing literature highlighted similar findings. Further studies are needed across other trauma and specialist centres to gain a better understanding of ABI neurorehabilitation needs, in order for a national pathway to be developed.

Poster 103
Characterising the temporal evolution of emotional and behavioural problems (EBP) in an Irish cohort of Autism Spectrum Disorder (ASD) affected children in early childhood.

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Objective: Children and adolescents with Autism Spectrum Disorders (ASD) frequently suffer from emotional and behavioural problems (EBP). Children with ASD have increased prevalence of internalizing (emotional) problems such as social difficulties, anxiety, depression; and externalising (behavioural) problems such as attention deficits, hyperactivity, and conduct disorders. The time of onset of behavioural problems in ASD is disputed, and varies depending on the severity of ASD. In a well-characterised ASD cohort, we aim to evaluate the temporal evolution of their emotional and behavioural development between 2 and 5 years of age.
Methods: Children with a confirmed ASD diagnosis were recruited from a longitudinal birth cohort study in Cork, Ireland. Using serial scoring from a well-recognised measure of internalising and externalising behaviours, the Child Behaviour Checklist (CBCL), we illustrate how the behavioural profiles of ASD affected children evolve over time, and help to identify when EBPs first develop.
Results: 34 children with ASD and 51 matched controls were included in the analysis. 76% (26/34) of the ASD group were of male sex. The average age at diagnosis of ASD was 4.97 years (SD 1.97). Six (18%) autistic children had a learning disability. We demonstrated significant evidence of emotional and behavioural problems at 2-year follow up across multiple domains (emotional reactivity, anxiety, and aggression). This worsened at 5-year follow up. Controls demonstrated no such early behavioural problems nor any deterioration in scoring over time.
Conclusion: The presence of higher EBP scores in younger age groups highlights the need to identify and treat these EBPs early. EBPs can persist and indeed worsen over time. Screening for EBPs should form part of routine ASD screening practice. We should support and educate the parents of children with ASD to address these EBP issues through family based therapies.

Poster 104

Neonatal unit admission, bilateral hearing impairment and neurodevelopment at two years of age

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Objectives: (1) To assess the impact of permanent bilateral hearing loss (BHL) on the neurodevelopment at the age of two years of children with a history of neonatal intensive care unit (NICU) admission. (2) To assess the prevalence of additional congenital anomalies in this group of children.
Methods: The local neonatal database was used to identify all babies admitted to the NICU (2008–2019) and subsequently diagnosed with BHL. They were matched for sex, birthweight and gestational age with a control group of children who had spent >48 hours on NICU but had normal hearing.
Data regarding developmental outcomes at two years' corrected age in both groups were obtained using the BadgerNet database, together with data regarding congenital anomalies and ongoing health issues.
Results: 44 babies met the inclusion criteria; full dataset available for 38. Development: At two years of age, statistically significant differences ($p<0.05$) exist between the group with BHL and the control group for neuromotor disability, global developmental impairment and impaired communication. Babies with BHL were also more likely to have ongoing respiratory, gastrointestinal and renal issues and were three times more likely to have a diagnosis of cerebral palsy but statistical significance was not reached. Congenital anomalies were significantly more prevalent in the group with BHL compared with the control group ($p<0.05$).
Conclusions: Children with BHL and a history of NICU admission present with an increased risk of moderate - severe neurodevelopmental impairment at the corrected age of two years compared to matched controls, predominantly in communication and neuromotor skills. They also have an increased likelihood of other congenital anomalies, at least some of which are likely to have wider health impacts and thus may compound the effect of the hearing loss on early developmental progress.

Poster 105

Indicative factors for possible genetic aetiology within a cohort of children with cerebral palsy

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This study investigated the indications for genetic testing within a cohort of children with cerebral palsy (CP) patients by identifying possible cases of atypical CP. One hundred and nine children in the South Cambridgeshire population cohort who had a clinical diagnosis of CP, with no known genetic diagnosis, were assessed for 7 features consistent with atypical CP. These features had been highlighted within a parallel project reviewing literature and the clinical record of a group of 11 children with known genetic cause for cerebral palsy within region. The features identified were normal gestation and delivery, epilepsy type or severe intellectual disability out of keeping with presentation, congenital abnormalities, dysmorphic features, atypical MRI findings and a family history. Each of these features was attributed a score of 1. Each patient was then given a score out of 7. Of the 109 patients, 25 (22.9%) were aged 0–5, 38 (34.9%) were aged 6–11 and 46 (42.2%) were aged 12–19. We found 9/109 patients (8.3%) had 3 or more features, 29/109 (26.6%) patients had 2 or more features, and 70/109 (64.2%) had 1 or more features. Of the 9 with 3 or more features, 1 patient had 4 features and 2 patients had 5 features. We concluded that a score of 3 or more on this assessment was a pragmatic threshold to consider genetic testing in children with CP.

Poster 106

WHO caregiver skills training programme has developed the social relationship and reciprocity, communication and behaviour patterns of children with ASD

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Objectives: The purpose of this study is to evaluate the effect of the WHO Caregiver Skills Training Programme on social relationships and reciprocity, communication and behaviour patterns of children with ASD age 2 to 9.
Method: The research design was a pre and post-test, by analysing the levels of 50 children with ASD age 2 to 9 from West Bengal (i.e. 25 children, whose parents have undergone the WHO Caregiver Skills Training and also the other 25 children, those who went through the treatment as usual who haven't undergone the training). Measures through the Indian Scale for Assessment of Autism (ISAA-40 Item) which analyzed the difference of the score of both the groups of children. The children whose parents received WHO-CST training over 9 weeks followed strategies in their everyday activities. The tools were delivered at the beginning and at end of the WHO-CST.
Results: WHO Caregiver Skill Training programme was found to be effective to decrease ISAA scores in social relationships and reciprocity, communication and behaviour patterns of children with ASD.
Conclusion: This study suggests that young children with ASD improve their life skills by participating in the WHO-CST program through their parents. Further studies are needed to establish casual relationships.

Poster 107

NICE Scholarship: Gap analysis of transition pathway and care of children and young adults with cerebral palsy in the South East

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Objective: At Evelina London Children's Hospital we provide tertiary care for children with Cerebral Palsy (CP) across south

London, Kent, Sussex and East Surrey. We currently also support an increasing number of adults with CP due to a lack of appropriate neurodisability services to transition them onto. This study aims to develop improved transition and access to services for young adults with CP.
Methods: The NICE guidelines and quality standards on: CP in under 25s, CP in adults, and Transition from children's to adults' services were used to develop questionnaires circulated to paediatric and adult health care providers (HCP). These included questions regarding current transition, capacity to deliver care and barriers to providing care according to these standards. A questionnaire to young adults with CP and their families evaluated their experience of transition, access to services, the challenges with care, and their needs from HCP. A focus group with parents of adults with CP and interviews with adults informed design of an ideal transition pathway and adult service.
Results: HCP reported: (1) Lack of awareness of NICE guidelines, and specific quality statements; (2) Variability in the transition pathway across the region; (3) Inequity of care across the SE with lack of services for adults with CP, particularly, those without a learning disability. Young adults and families reported: (1) Lack of knowledge about CP and associated co-morbidities from HCP in adult services. (2) Challenges accessing medication and referrals to specialist services by GPs. (3) Fragmented adult services with no 'ownership or responsibility' for holistic care.
Conclusions: (1) Significant challenges identified with transition pathways, and adult care across the region with non-adherence to NICE quality statements. (2) Continuing paediatric models of care (e.g. the Cerebral Palsy Integrated Pathway) into adult HCP will improve care. (3) Current business planning to create a regional young adult CP service.

Poster 108
Neonatal unit admission, unilateral hearing impairment and neurodevelopment at two years of age

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Objectives: To assess the developmental outcomes of children with unilateral hearing impairment (UHL) and a history of Neonatal Intensive Care Unit (NICU) admission, with the aim to inform future research on producing clinical management guidelines.
Methods: This retrospective, descriptive study analysed 25 children with UHL and a NICU admission. Developmental outcomes at age two years were collected from NHS databases and compared to outcomes of matched controls (NICU admission but no hearing loss). Analysis included chi-squared tests, or Fischer's exact tests if $n<5$.
Results: Children with UHL and a NICU admission were statistically more likely than their matched counterparts to have impaired communication ($p<0.001$), congenital anomalies ($p<0.001$), craniofacial anomalies ($p=0.004$) or developmental impairment ($p=0.01$). A higher prevalence of neurological and spinal (32%), gastrointestinal (28%) and vision and eye (24%) issues were identified compared with the control group but statistical significance was not reached. Comparison within the UHL cohort revealed patients with developmental impairment were statistically more likely to have multiple congenital anomalies ($p=0.019$) or have trialled a hearing device ($p=0.019$).
Conclusion: Children with UHL and a NICU admission are at high risk of certain adverse anatomical and behavioural outcomes. Having multiple congenital anomalies may suggest closer developmental monitoring and support is needed. This study begins to identify a constellation of features associated with this unique population and highlights the need for further research to produce clinical management guidelines to ensure consistent high-quality care.

Poster 109
Spectrum of neurosurgical interventions in patients attending a community paediatric clinic in Northern Ireland

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Objectives: Children with a wide range of neurodisabilities attend community paediatric clinics with multidisciplinary input. A few patients require elective and sometimes urgent neurosurgical interventions. The aim of this study was to look at a selection of children, their pre-existing diagnoses and the spectrum of neurosurgical interventions they required.
Methods: A retrospective review of our outpatient database was carried out and 14 cases were selected for this study.
Results: There were equal number of male and female children with age ranges from 17 years to 4 months. Two of the ex-preterm infants with cerebral palsy and four limb movement disorder underwent selective dorsal rhizotomy (SDR) and the third child had deep brain stimulation (DBS) for severe dystonia. Another child with ADCY5 mutation had multiple DBS and later scoliosis surgeries. Two patients with intractable epilepsy associated with lissencephaly and schizencephaly with COL4A1 mutation had vagal nerve stimulators (VNS). The latter also needed a hemispherotomy. Among the two children with myelomeningocoeles and unshunted hydrocephalus, one needed urgent repair of the sac at delivery. A third child with OEIS complex (omphalocoele, exstrophy of bladder, imperforate anus and spina bifida) required extensive neurosurgical intervention including VP shunt and instrumentation for scoliosis. Two other children had VP shunts for posterior fossa tumour and post infectious hydrocephalus. A four month old with a large posterior fossa cyst and extensive hydrocephalus needed a VP shunt and later endoscopic fenestration of the cyst. A child with Down syndrome had C1-C2 vertebral fusion surgery, and then had Moya Moya disease with TIAs and stroke, which resolved.
Conclusion: The paediatrician will need to recognize problems as they arise so that timely referrals can be sent to tertiary teams. Familiarity with some of the neurosurgical interventions and their complications may aid in appropriate counselling of families.

Poster 110

The effects of WHO caregiver skills training on psychological well-being and depression of parents of children with ASD

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Objectives: The purpose of this study is to evaluate the effect of a parent-mediated intervention WHO Caregiver Skills Training Programme on depression and psychological well-being of parents of children with ASD age 2 to 9.
Method: The research design was a before-after study, by analysing the mental health status of parents (both mother and father) of 40 children with ASD from West Bengal (i.e. parents of 20 children who have undergone the WHO Caregiver Skills Training and 20 treatment as usual who haven't undergone the training). Measures included Ryff's Psychological Well-Being Scales (PWB), 42 Item versions which measure six aspects of wellbeing and happiness: autonomy, environmental mastery, personal growth, positive relations with others, purpose in life, and self-acceptance. Beck Depression Inventory was used for depression. The parents who received WHO-CST training over 9 weeks followed strategies in their everyday activities. The tools were delivered at the beginning and at end of the WHO-CST.
Results: WHO Caregiver Skill Training programme was found to be associated with positive changes in psychological well-being and also reducing depression of parents of children with ASD.
Conclusion: This study suggests that parents of young children with ASD improve their well-being by participating in the WHO-CST program. Further studies are needed to establish casual relationships.

Poster 111

Retrospective casenote audit of fracture incidence and cause within a neurodisability service

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Objective: The Nottinghamshire neurodisability community service provides treatment for a large number of non-ambulant children with complex neurodisability. In 2019 a significant number of fracture incidences were identified within this population. The aim of this audit was to assess fracture figures over a longer period of time, and identify any causality contributing to these fractures. Furthermore, any correlation between physiotherapy and fractures would be identified.
Method: A retrospective case note audit was conducted for all known fractures within the service over a 10 year period (2010–2020). Fractures were identified through submitted incident reports. All patients were unable to stand or mobilise without assistance. Fractures within mobile children or children not predisposed to osteopenia were excluded. Children with osteogenesis imperfecta were excluded due to the increased incidence of fractures.
Results: A total of 30 fractures within 18 different patients met the inclusion criteria for the audit. The majority of fractures were identified as being due to manual handling procedures (43%). Within a significant number of fractures, the mechanism remained unknown (33%). In many of these cases the fracture was not identified at the time it was sustained. Despite one child suffering 5 fractures throughout the period, there were no occasions throughout the identified fractures, where the cause of the fracture recurred. There were no identified incidences where physiotherapy intervention correlated with the occurrence of the fracture.
Conclusion: There is a high incidence of osteopenia within children equivalent to GMFCS level 5. This puts this identified population at a significant risk of fracturing through non-traumatic incidences. This audit identifies manual handling procedures as a significant cause of fractures. Although in a large percentage of fractures the modality remains unknown, it would be difficult to establish the causality in cases where symptoms of a fracture have not presented for a period of time.

Poster 112

How paediatricians investigate early developmental impairment: a qualitative interview study

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Objective: Determining factors influencing paediatricians' choice of investigations for early developmental impairment (EDI).
Methods: A qualitative descriptive study using semi-structured qualitative interviews of paediatricians working in Child Development and Paediatric Neurology units in England. 9 Consultant Community/Neurodisability Paediatricians, 1 General paediatrician with expertise in neurology, neurodisability and epilepsy, 1 General paediatrician, 3 Paediatric Neurologists were recruited to have a semi-structured interviews in person or online. Thematic analysis included familiarisation of data, initial coding of all data using an inductive approach by two researchers, review of initial codes, agreement on a coding structure for the whole dataset, and identification of a thematic structure to determine main and subthemes. Themes were developed using an iterative process to capture all range of views.
Results: Two themes emerged during analysis. The value of an aetiological diagnosis outlined why clinicians wanted to help families find an aetiology. Managing risk and probability when investigating EDI explored attitudes towards choice of investigation and contained 4 subthemes. 'Circumspection' involved blanket investigations chosen irrespective of phenotype and high regard for guidelines, standardisation of practice, and a fear of missing a diagnosis. This was thought to represent inexperience. 'Accepting appropriate risk' involved participants choosing investigations based on clinical phenotype, recognising some aetiologies would be missed. Invasiveness of investigations and treatability were important, but cost, whilst reported to be important, may not have been a significant factor. Consultants found they 'transitioned between practices' during their career, though they retained characteristics of both. 'Improved practice' was thought possible with better evidence on how to stratify investigations based on phenotype.
Conclusions: There are many factors that influence paediatricians' choice of aetiological investigation in EDI, but clinical factors are the most important. Paediatricians want better evidence to allow them to select the right investigations for each child without a significant risk of missing an important diagnosis.

Poster 113

End of life symptom burden and management in children with neuro-disability

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Objectives: To determine the incidence of complex symptoms in children at end of life with neuro-disability
Methods: A single centre retrospective observational study in Cork University Hospital between January 2016–May 2019. Children between 0–16 years with an underlying neuro-disability who had been referred to the palliative care team and died in hospital or had an in-patient stay within one month of their death were included.
Results: Fourteen children were included, with a median age of 11.2 years at death. 35.7% died in their own home. This lower than national average of home deaths was felt to be attributed to the exclusion of oncology patients as they were not cared for in our centre. Children experienced a significant symptom burden, specifically neurological, gastrointestinal and respiratory symptoms. 85.7% had a background of epilepsy, with over half having difficult to control seizures requiring multiple medications and routes of administration. Agitation and irritability were reported in 50% and over 70% of children with these symptoms also had difficult to control seizures. Poor gut health hindered absorption of medications, limited routes of administration and subsequently led to the deterioration of symptom control. Respiratory symptoms were prevalent in 92.3% of cases and ultimately the most common cause of death. A collaborative team approach was evident in the care of each patient with all having input from allied health care and over 70% receiving input from consult teams.
Conclusion: Optimisation of symptom control can be hugely challenging but should always be possible, in the patient and carers preferred place of care. Access to specialist palliative care services should be early in disease trajectory and should be equitable. Palliative care aims to help ordinary people who find themselves and their families in extraordinary situations. Our goal must forever be to ensure each child lives and dies well.

Poster 114

Service evaluation of blended diet by gastrostomy

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The prevalence of gastrostomy feeds is increasing in the paediatric population. Commercial feeds are frequently used, due to concerns that home-made blended feeds may be nutritionally incomplete, increase the risk of stoma infections, tube blockages, etc. Families, however, are increasingly using blended home-made foods over commercial feeds, with reports that blended diet has positive clinical and family consequences. At Bolton NHS Foundation Trust, 17 of 110 (15.5%) paediatric patients on home enteral gastrostomy feeds are using blended diet. We administered a semi-structured questionnaire to the parents of paediatric patients on blended diet by gastrostomy feeds. The mean age of patients at the time of data collection was 7 years and 3 months, with a mean duration on blended diet of 27 months. Caregivers reported a statistically significant improvement in feed-associated symptoms after implementing blended diet, and a positive impact on the child and family. Staff at special schools similarly reported positive outcomes with blended diet, and an improvement in attendance and school engagement. This service evaluation highlighted areas where we can better support families choosing to use blended diet. First, we must educate clinicians and school staff in blended diet and signpost to appropriate training to improve support in the educational, community, and hospital setting. Second, hospitals and schools should have appropriate facilities to prepare and administer blended diet safely. Third, caregivers need education on pragmatic aspects such as choosing a blender, gastrostomy equipment, nutritional content of feeds, feed volume, rate, and consistency. In conclusion, blended diet can not only support the child nutritionally, but has other holistic benefits, such as facilitating inclusion in family meals and events. Evaluating our local service helped us understand our population and to better support children and caregivers in making a choice that is right for their family.

Poster 115

A case of pyridoxine dependent epilepsy, presenting with features of Autism Spectrum Disorder (ASD)

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Introduction: Pyridoxine Dependent Epilepsy, usually presents as seizures immediately after birth but can present in utero, months or years after birth. It is a rare autosomal recessive disorder, caused by homozygous or compound heterozygous variants in the ALDH7A1 gene. Along with seizures, intellectual disability, delay in executive functioning and visual- spatial function have also been observed. We present a case of Pyridoxine dependent epilepsy with features of ASD.
Materials and Methods: The proband is a 4-year-old male child born to phenotypically healthy parents with a consanguineous marriage. Mother had three miscarriages before the index child. He developed convulsions at 6 months of age which responded to anticonvulsants and pyridoxine supplementation. There are no convulsions in past 2 years with normal MRI and BERA reports. Child has features of developmental delay in motor, speech-language milestones and toilet-training. He also has features of ASD in form of social-communication deficits and restrictive/repetitive pattern of interests (echolalia, difficulty in transitions, preoccupation with vehicles, toe walking) as per DSM-V criteria. Whole Exome Sequencing was performed to identify the cause.
Results: A likely pathogenic homozygous, missense variant, c.1232C>T (p.P411L) in exon 14 of ALDH7A1 gene (ENST00000409134.3) was identified. Parental segregation by Sanger sequencing showed both parents to be heterozygous carriers. The identified variant has previously been reported in patients affected with pyridoxine-dependent epilepsy (SCV001409363.2).
Conclusion: Pyridoxine Dependent Epilepsy is known to respond to pyridoxine treatment. Dietary modifications in form of reducing dietary lysine and supplementing arginine has shown promise in improving intellectual disability. The present case supports the association of Autism phenotype with the disorder, and need for further study and evaluation of treatment options to improve quality of life both for the child and the family.

Poster 116

Hippocampal maldevelopment associated with sudden death: An underrecognized cause of sudden unexpected death in childhood?

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We describe a case of sudden death in a 3-year-old male with a history of febrile seizures and hippocampal maldevelopment found on post-mortem. He was born at term by normal delivery. From 1 year of age he had typical febrile seizures, with otherwise normal development, good health, and no relevant family history. A few days prior to his death he had a cough, coryza, and low-grade temperature. On the day that he died he was pyrexial and was later found unresponsive and asystolic in the prone position. Post-mortem virology was positive for rhinovirus/enterovirus, adenovirus, and bordetella parapertussis, suggestive of incidental or on-going viral infection. Brain histology demonstrated dentate gyrus bilamination, hyperconvolution and granule hetertopia. The paediatric pathologist gave the cause of death as hippocampal maldevelopment associated with sudden death (HMASD). Sudden unexpected death in infancy and childhood (SUDI/SUDC) is a descriptive term encompassing all unexpected deaths in infants and children, including those where a cause is ultimately identified. Sudden unexplained death in childhood (SUDC) describes death in a child older than 1 year of age that occurs suddenly and remains unexplained after a thorough review and investigations. We describe three publications by Dr Hannah Kinney and colleagues, who found an association between sudden unexpected death in childhood and prone discovery, sleep period, individual or family history of febrile seizures and hippocampal maldevelopment. We believe that HMASD is an underrecognized cause of sudden unexpected death in infancy and childhood (SUDI/SUDC) and would like to raise awareness of this differential diagnosis for SUDI/SUDC.

Poster 117

[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.]

A female infant with episodic movements

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Poster 118

Lentiviral haematopoietic stem and progenitor cell gene therapy for metachromatic leukodystrophy (MLD): Clinical outcomes from 38 Patients

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Objective and Methods: MLD is a fatal demyelinating lysosomal storage disease resulting from arylsulfatase A (ARSA) deficiency. Thirty-eight patients with early-onset MLD (20 late infantile [LI], 18 early juvenile [EJ]) were treated with haematopoietic stem and progenitor cell-based gene therapy (atidarsagene autotemcel, "arsa-cel"), consisting of autologous CD34+ cells transduced ex vivo with a lentiviral vector encoding the functional human ARSA gene. Following myeloablative busulfan conditioning, arsa-cel was administered intravenously. Key endpoints were compared to an untreated natural history (NHx) cohort.
Results: Of 38 patients with 1 month to 7.9 years of follow-up, 35 are alive; 2 died from disease progression, 1 from cerebral stroke, all unrelated to arsa-cel. There were no treatment-related serious adverse events, malignancies, abnormal clonal expansion, or evidence of replication-competent lentivirus. All patients achieved haematological recovery. Stable engraftment of gene-corrected cells and restoration of ARSA activity in the haematopoietic system and cerebrospinal fluid was observed in all patients with ≥3 months follow-up. The majority of patients treated pre-symptomatically maintained long-term walking capability and normal cognitive development. Additionally, early-symptomatic EJ patients treated before entering the phase of rapid decline (able to walk independently, with IQ≥85 at baseline, and without clinical deterioration between screening and treatment), showed better motor and cognitive scores or slower rate of decline versus NHx.
Conclusions: Data from 38 early-onset MLD patients with up to 7.9 years of follow-up demonstrated that arsa-cel was generally well-tolerated and effective in modifying the disease course of early-onset MLD. Arsa-cel (tradename: Libmeldy™), was approved by the European Medicines Agency in 2020 and is indicated for the treatment of children with LI or EJ forms without

clinical manifestations of the disease, and in children with the EJ form, with early clinical manifestations of the disease who still have the ability to walk independently and before the onset of cognitive decline.

Poster 119

The expanding genetic spectrum of alternating hemiplegia of childhood-like disorders: looking further than ATP1A3

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Objective: Alternating Hemiplegia of Childhood (AHC) is a rare neurological disease, characterized by paroxysmal episodes of alternating weakness. Previously, clinical criteria were used to establish diagnosis, until identification of the first causative gene, ATP1A3. Only 75–85% of cases can be attributed to ATP1A3 variants, suggesting a wider spectrum of genes causing AHC-like disorders.
Methods: Patients with AHC-like disorders without ATP1A3 variants were identified in the AHC and Neurogenetic Movement Disorder clinics at Great Ormond Street Hospital. Molecular genetic diagnosis was achieved through research whole genome sequencing. Clinical data was collected through retrospective case note review.
Results: We identified 5 patients with pathogenic mutations in 4 different genes. Patient 1 has a typical AHC phenotype fulfilling all classical clinical criteria. He had onset of paroxysmal episodes at age 4 months (hemiplegic and plegic events with some improvement after sleep), further paroxysmal events (dystonic, autonomic, epileptic), persistent neurological symptoms (dystonia, ataxia), and developmental delay. He carries a de novo heterozygous variant in UBE3A (c.2625_*11del). Patients 2 and 3 also fulfil clinical criteria for typical AHC except for improvement in sleep. Patient 2 carries biallelic pathogenic TBC1D24 variants (c.457G>A;c.680G>T), whilst patient 3 was diagnosed with a de novo heterozygous variant in RHOBTB2 (c.1532G>A). Patients 4 and 5 are less typical; Patient 4 with the same RHOBTB2 variant has episodes of whole-body weakness, as well as dystonia, epilepsy, and developmental delay. Patient 5 suffers from paroxysmal hemidystonic episodes with cognitive impairment and carries a de novo novel homozygous frameshift variant in JPH3 (c.1310del).
Conclusions: AHC shows clear genetic heterogeneity, and a broad spectrum of neurodevelopmental genes are implicated in disease pathogenesis. Novel gene identification will enable the curation of appropriate gene panels to optimise diagnostic testing.

Poster 120

Yield of whole genome sequencing with heteroplasmy in mitochondrial disorders

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Objectives: Mitochondrial disorders are caused by nuclear (nDNA) or mitochondrial (mtDNA) mutations, the latter exhibiting heteroplasmy. We describe a case where consultant paediatric neurologists (CPN) were unaware of the variability in reporting mtDNA variants. We surveyed three teams, to identify understanding and training needs.
Case: A previously well eight-year-old female presented with recurrent headache, vomiting and focal motor seizures. Plasma lactate was 2.9mmol/L and MRI T2/FLAIR showed white matter hyperintensities. mtDNA sequencing revealed a m3955G>C MT-ND1 variant in blood (13% heteroplasmy), urine (46%) and skeletal muscle (82%), leading to diagnosis of Mitochondrial encephalomyelopathy lactic acidosis and stroke-like episodes (MELAS) syndrome. Initial gene-agnostic whole genome sequencing (WGS) had identified this variant but it was unreported as it fell below a 20% threshold. Awareness of such thresholds and testing variability was hence key to diagnosis. Three routes exist for mtDNA variant testing: Exeter's whole exome (WES) testing, the regional genomic laboratory hub (GLH) whole genome (WGS) testing, and mitochondrial centre-based WGS. Mitochondrial variants detected above 5% are tiered in GLH WGS and reported. Variants are often unreported by WES as its sensitivity for heteroplasmy is unknown.
Methods: A seven-question survey was sent to CPNs in three UK centres, to assess awareness of heteroplasmy reporting in WES and WGS.
Results: 15/21 CPNs responded. Most believed nDNA variants were reported by WES and WGS (87% and 80%). Regarding WES, 67% did not think mtDNA variants were reported; 47% were unsure if a threshold was used. Regarding WGS, 47% thought mtDNA variants were reported; no consensus was found regarding use of a reporting threshold.
Conclusions: Reporting of mtDNA variants is limited by knowledge of thresholds and variability. We recommend discussion between CPNs and laboratories on specifics of different technologies. Finally, clinical phenotype is key: results must be reviewed within an individual's clinical context.

Poster 121

Alpha-fetoprotein values in children with Ataxia-Telangiectasia increase with age

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Objectives: Serum alpha-fetoprotein (AFP) is known to be raised in A-T, and we previously reported values in children attending the national children's A-T clinic (RCPCH 2021). We wanted to see how these compared with previous publications, and how they changed with age.
Methods: The national A-T children's clinic paper and digital records were reviewed from 2006–2019 and clinical and AFP data extracted. A systematic review was carried out searching 5 databases: Ovid SP (Medline), EMBASE, Web of Science, PubMed, Scopus, and the Cochrane Library.
Results: Complete data was available for 77 clinic children with A-T, including 6/77 (8%) with mild variant A-T. They were aged 0

to 16.9 years, including 39/77 (51%) males, and 6/77 (8%) with cancer. There were 251 clinic serum AFP measurements from 4–1107 kU/L in patients under 20 years of age [reference range 0.7–7.3 kU/L]. AFP increased with age up to 20 years, from a median of ~100 in 0–5 year-olds to a median ~450 in 15–20 year-olds. The same was true in the systematic review of 64 cases reported in the literature, including 5/64 (8%) with mild variant A-T. We had longitudinal data on 38 clinic patients with 3 or more AFP values, which similarly increased from 0–20 years.

Conclusions: Data from the systematic review, and from the time-trend analysis has not been previously reported. A single raised AFP is common and not indicative of cancer in children with A-T. AFP rises with age in childhood, so we developed a centile chart of AFP values in children with A-T without cancer to age 20 years. The 6 children with cancer had values between the 5th and 90th centiles.

Poster 122

Neurodegeneration with brain iron accumulation (NBIA) in UK children with progressive intellectual and neurological deterioration (PIND)

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Objectives: To evaluate UK children with PIND diagnosed with NBIA.

Methods: The PIND study has been conducted through the British Paediatric Surveillance Unit since May-1997. Patients <16 years with PIND are identified via monthly notifications sent to all UK consultant paediatricians. Clinical details are evaluated by an independent expert group.

Results: By Sept-2021, of the 2107 PIND children with a known underlying diagnosis, 90(4%) had NBIA. 49(54%) had PLA2G6-Associated Neurodegeneration(PLAN) of which 10 were diagnosed clinically as Infantile Neuroaxonal Dystrophy prior to PLA2G6 gene testing; 38(42%) had Pantothenate Kinase-Associated Neurodegeneration(PKAN) of which 11 were diagnosed clinically as "Hallervorden-Spatz disease" (term now redundant) prior to PANK2 gene testing; 3(3%) had Beta-propeller Protein-Associated Neurodegeneration(BPAN) with WDR45 mutation. There was earlier diagnosis with time (mean age at diagnosis: 8.5 years if born before 2011, 4.0 years if born after 2011). NBIA patients share common features; motor/cognitive regression, abnormal tone and eye abnormalities are reported in 90%.

Mean age at first symptom varied according to NBIA subtype (BPAN=1.4years, PLAN=1.6years, PKAN=3.5years), most commonly with developmental delay (71%PLAN, 100%BPAN) and walking difficulties (50%PKAN). 90% of NBIA patients had evidence of iron on neuroimaging by 8.5 years. Compared to PKAN, fewer PLAN patients (30% versus 73%) had features of iron on neuroimaging, possibly related to younger age at imaging (3years versus 8years). 53/85(62%) of children died during the study (mean age=13years) varying according to NBIA subtype (60% PLAN, 40%PKAN, 0%BPAN).

Conclusions: NBIA is an important cause of childhood PIND and a genetically and phenotypically diverse group. There is under-representation of BPAN cases because neuroregression becomes more evident in adulthood. Genomic advances have facilitated earlier diagnosis, crucial for this group of life-limiting, neurodegenerative disorders as novel, precision therapies are in advanced translational stages.

Acknowledgements: Funded by the NIHR Policy Research Programme (PR-ST-1216-10001). Views expressed are not necessarily those of DoH.

Poster 123

Drosophila behavior as a tool for exploring human neuropsychiatric symptoms: the example of the TCF4-related genes pleiotropy

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Objective: A variety in genetic phenotypes for the same gene is often referred to as pleiotropy. Loss of function in human genes TCF4, NRXN1, CNTNAP2, and ERC2 is associated with a variety of symptoms leading to different diagnoses including epilepsy, intellectual disability, autism, schizophrenia, and ADHD. Using Drosophila as an experimental tool, it has been possible to recognize behaviors such as night hyperactivity and habituation defect as phenotypes of, respectively, ADHD and autism-related genes. We aim at determining, in Drosophila, whether phenotypic pleiotropy is present for a group of genes. We will use this behavior paradigm to further expand our understanding of the neural basis of neuropsychiatric semiology.

Methods: We built a hypothetical genetic network involving TCF4, NRX1, CNTNAP2, ERC2, ERB4, and a possible downstream regulatory molecular mechanism, the EGFR signaling pathway. In order to access in vivo the function of the referred genes, we conditionally knocked down their Drosophila orthologs, Da, Nrx1, NrxIV, Brp, and Egfr. We used the automated light-off jump habituation paradigm and Drosophila Activity Monitoring systems to characterize habituation, activity, and sleep. In order to further explore the role of EGFR/ERK, the larvae were exposed to Biochanin A.

Results: Knockdown of any of the tested genes gave rise to habituation, sleep, and activity phenotypes. Two main non-overlapping behavior phenotypes were defined, with night hyperactivity and normal habituation opposing excessive sleep and decreased habituation. Pharmacological modulation of EGFR/ERK signaling by exposure to Biochanin A changed habituation as did genetic knockdowns.

Conclusions: Phenotypic pleiotropy was successfully reproduced in Drosophila for this group of genes. Quantitative changes in EGFR/ERK appear as key regulators affecting all the genes in the network, driving behavior along a spectrum between the two defined phenotypes. We propose to determine the clinical relevance of this work by searching in patients for the aforementioned behavior traits.

Poster 124

Children with Juvenile Huntington Disease (JHD) in the UK - clinical and diagnostic features.

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Objective: To review children with JHD in a UK study of children with progressive intellectual and neurological deterioration (PIND).
Methods: Since 1997 the Study has performed prospective epidemiological surveillance of UK children aged <16 years with PIND, via the British Paediatric Surveillance Unit.
Results: Between May 1997 and August 2021 29 children with JHD were identified (13f,16m). Ethnicity was: White 22, Indian 1, unknown 6. Family history of HD: father 25, mother 2, unknown 2. Age of onset (n=28): 2y-13y (median 6y). Age at diagnosis (n=29): 3y 6m-15y 6m (median 10y). Age at death (n=24): 5y 3m-24y (median 12y 8m). Onset-diagnosis (median): 4y. Onset-death (median): 6y 8m.
In 2019 there were 12.7 million UK children aged <16 years and at that time 6 PIND Study JHD children were alive, giving a point prevalence of 0.47/1,000,000. Commonest symptoms/signs (more than one/child). At presentation: co-ordination/motor/gait problems 18, speech/language/learning difficulties 18, cognitive decline 7, abnormal behaviour 6. Subsequently: intellectual difficulties/deterioration 28, abnormal behaviour 22, abnormal gait 20, dysphagia/dribbling/dysarthria 16, rigidity 15, seizures 15, co-ordination problems 12, tics/tremor/jerking 11. Investigations. CT brain scans n=4, atrophy caudate nucleus: 1. MRI brain scans n=17, atrophy and/or high signal in caudate nucleus: 8. Genetic confirmation: yes 24, no 4, unknown 1.
Conclusions: The PIND Study gives a unique view of JHD, highlighting early onset in some - 9 first developed symptoms before age 5y; the youngest age at diagnosis was 3y 6m. After onset the median time to diagnosis was 4y and to death was 6y 8m (relative rapid progression compared to adults). Brain imaging may be helpful but the key to diagnosis is family history and demonstration of increased CAG repeats in the HTT gene.
Acknowledgements: Funded by the NIHR Policy Research Programme (PR-ST-1216-10001). Views expressed are not necessarily those of DoH.

Poster 125

Evaluation of the 100,000 genomes project for paediatric neurogenetic conditions in the East London population

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Objective: Paediatric neurogenetic disorders have wide phenotypic and genotypic heterogeneity, and traditional genetic testing is frequently not diagnostic. Recent findings have shown an increased diagnostic yield using whole genome sequencing (WGS). The objective of this study was to perform whole genome sequencing, as part of the 100,000 Genome Project, for paediatric patients with undiagnosed neurological disorders in Tower Hamlets, and assess the diagnostic yield.
Methods: We approached 34 families and recruited 33 families (110 individuals) with undiagnosed neurological disorders at the Royal London Hospital in Tower Hamlets. Patients were included if they were under 18 and had symptoms of a neurological disorder, with no diagnosis after initial investigations. WGS was performed as part of the 100,000 Genome Project.
Results: All families invited to join the cohort, except one, accepted to join the study. The most common ethnic group of patients was Bangladeshi (51.5% of the cohort). In addition, 45.5% were born to consanguineous parents. In total, 72.7% of patients presented with a movement disorder, of which dystonia (36.4%) was the most common, followed by hypotonia (24.2%). Pathogenic variants in different genes were discovered in 21.2% of probands. 42% of the pathogenic mutations in our population were homozygous and these all occurred in consanguineous families. These included homozygous missense mutations: in SERAC1 causing dystonia and developmental regression, NDUFV1 mutation dystonia and spasticity, and AP4M1 causing focal seizures and developmental delay.
Conclusions: The results of this study demonstrate an important role for WGS in the diagnosis of paediatric neurological disorders in our east London population.
Acknowledgements: This research was made possible through access to the findings generated by the 100,000 Genomes Project; http://www.genomicsengland.co.uk.

Poster 126

Impact of whole genome analysis on diagnostic delay in children with probable monogenic neurological disorders

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Objective: Neurogenetic disorders in children present diagnostic challenges. Factors underlying this include overlapping phenotypes, variable expressivity and pleiotropy within a single disease entity. Next-generation sequencing has strengthened diagnostic pathways in the past decade, leading to quicker time-to-diagnosis. We assessed the impact of whole genome sequencing (WGS) as a primary diagnostic method on time and resource utilization in children with early, severe neurological disease.
Methods: The Next Generation Children's Project (NGC) investigated the yield of rapid trio WGS. We identified a subgroup of 83 children who were referred to the project by the paediatric neurology team. We divided the group into those in whom the paediatric neurology team had received the referral prior to WGS becoming available, and those in whom referrals were received once it was accessible. Children were considered for NGC when prior investigations had not yielded a diagnosis, there was a likely monogenic disorder, and parents consented to trio testing. A subset analysis of all children with a non-epileptic WGS-based diagnosis is reported here.
Results: Referral dates ranged from several years prior to the study onset (pre-2018 group) to referrals after WGS became available (2018 onwards group). 10 children were diagnosed with a non-epileptic disorder by WGS, including ataxia, microcephaly, mitochondrial, motor and neurodegenerative disorders. 6 of 10 children were referred to the department prior to WGS availability. On average, the pre-2018 group underwent an average of 20

investigations (50% of the local protocol) prior to WGS results while the 2018 group underwent an average of 6 investigations (21%) prior to WGS results.
Conclusions: Children who were provided with WGS earlier in their diagnostic journey underwent considerably fewer investigations. Rapid genomic investigations also reduced time-to-diagnosis, increased opportunities for early interventions, and enabled families to access diagnosis-specific information and support.

Poster 127

Mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes (MELAS) syndrome: Single centre experience 2001–2021

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Introduction: Mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes (MELAS) syndrome is a rare mitochondrial disorder with neurological manifestations. It is most commonly caused by the m.3243A>G mutation in the mitochondrial gene MT-TL1. Patients typically present between two and 20 years-of-age with epilepsy, recurrent headaches, vomiting, hearing/visual impairment and stroke-like episodes. We reviewed all children diagnosed with MELAS at our centre (a tertiary UK paediatric neurology centre covering a regional population of nearly 5 million children) in 2001–2021. Five children were diagnosed with MELAS in this twenty year period age 6–15. 4 (80%) presented with episodic headache and vomiting. Seizures occurred in 3 (60%) and visual disturbance in 3 (60%). 4 (80%) had MRI changes (occipital and/or parietal, cortical and/or subcortical white matter changes not confined to a single vascular territory). Genomic diagnosis was achieved in all children – m.3243A>G in 3 (60%), m.3955G>C in 1 (20%), and m.3252A>G in 1 (20%). Blood heteroplasmy of variants where available varied significantly. In some cases of low blood heteroplasmy, muscle biopsy was required to make the diagnosis.
Discussion: MELAS in our population has presented in most cases with a highly recognisable phenotype, although there are notable exceptions - mitochondrial heteroplasmy and random mitotic segregation contribute to phenotypic variation. Due to this, careful phenotype-genotype correlation, awareness of limitations of genomic investigations and judicious use of invasive tissue sampling is particularly important. Although precision therapy is lacking, diagnosis improves management, enables cascade screening, and informs family planning decisions of female carriers.

Poster 128

Rapid exome sequencing for neonatal and paediatric patients at Royal London Hospital, Barts Health NHS Trust

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Objective: Rapid trio exome sequencing was commissioned by NHS England from 1st October 2019 for acutely unwell children with a likely monogenic disorder. Testing uses an inheritance based gene agnostic approach. The reported diagnostic yield for families tested to date at Exeter Clinical Laboratory is 27%. For couples with two or more pregnancies affected with a lethal prenatal or neonatal disorder, the diagnostic yield increases to 49%. Our objective was to review all cases referred for rapid exome sequencing from Royal London Hospital since October 2019 in order to evaluate our diagnostic yield and identify any common clinical features.
Methods: We reviewed the clinical notes for all patients referred for rapid exome sequencing. Using an audit tool, we identified presenting symptoms, family history, initial investigations, exome sequencing results and patient outcome.
Results: Eighteen patients were referred for testing; nine from the neonatal service and nine from paediatrics. All patients were referred following clinical assessment by paediatric neurology and discussion with clinical genetics. Exome sequencing identified a genetic cause in twelve patients; a diagnostic yield of 67%. Following diagnosis, two patients were commenced on treatment with significant therapeutic benefit. Palliative care input was sought for six patients. Where testing was diagnostic, 67% of our patients were born to consanguineous parents.
Conclusions: Our diagnostic yield is significantly higher than that reported by the laboratory which suggests our referral pathway is robust. The rate of consanguinity is reflective of our patient population (8.2% of all births) but also indicates that this should increase clinical suspicion of a monogenic disorder. Rapid exome sequencing has led to improved care of our acutely unwell patients; it has informed treatment options, surveillance investigations and re-direction of care. It has rapidly resolved the diagnostic odyssey for a number of families and has reduced the need for further investigations.

Poster 129

Safety, tolerability, and pharmacokinetics of eteplirsen in patients 6–48 months old with Duchenne muscular dystrophy amenable to exon 51 skipping

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Objectives: Eteplirsen is indicated for treatment of exon 51 skip-amenable patients with Duchenne muscular dystrophy (DMD). Previous studies in patients >4 years of age indicate eteplirsen is well tolerated and attenuates pulmonary and ambulatory declines compared with matched natural history cohorts. Our objective was to evaluate the safety, tolerability, and pharmacokinetics of eteplirsen in patients aged 6–48 months, the youngest population of patients with DMD in a clinical trial to date, in Study 4658-102 (NCT03218995).

Methods: In this open-label, multicenter, dose-escalation study, patients who have a confirmed mutation of the DMD gene amenable to exon 51 skipping (Cohort 1: aged 24–48 months, n=9; Cohort 2: aged 6 to <24 months, n=6) received ascending doses (2, 4, 10, 20, 30 mg/kg) of once-weekly eteplirsen intravenously over 10 weeks, continuing at 30 mg/kg up to 96 weeks. Endpoints included incidence of adverse events and clinically significant laboratory abnormalities (primary) and pharmacokinetics (secondary).

Results: All patients completed the study (N=15). Average time since diagnosis was 10.5 months, and most (13/15, 86.7%) were not taking corticosteroids. Eteplirsen was well tolerated with no treatment-related discontinuations, deaths, or evidence of kidney toxicity. Most treatment-emergent adverse events were mild, and the most common were consistent with those commonly seen in pediatric populations (pyrexia, nasopharyngitis, vomiting, cough, diarrhea). Eteplirsen pharmacokinetics were consistent between both cohorts and aligned with expectations based on previous clinical experience in males with DMD older than 4 years of age.

Conclusions: These safety and pharmacokinetic results contribute to the body of evidence supporting the early use of eteplirsen in males with DMD.

Poster 130

A novel genotype-phenotype relationship in neonatal-onset CAD deficiency: a case report

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Introduction: CAD is a multi-enzymatic protein involved in de novo pyrimidine biosynthesis. CAD deficiency (OMIM #616457) is an autosomal recessive condition associated with global developmental delay, dyserythropoietic anaemia, and refractory epilepsy, which is highly responsive to uridine supplementation. Due to limited documented cases of this highly heterogenous condition, the full clinical spectrum of CAD deficiency remains elusive, hindering diagnosis and treatment.

Clinical findings: We present a female infant with complicated perinatal history (C-section for placenta praevia, forceps delivery, and NICU admission due to shock), whose MRI head at 1 week of age showed extensive neurological abnormalities, including microcephaly, ventriculomegaly, periventricular cysts, and an immature gyral pattern. At 3 weeks of age, she exhibited tonic-clonic seizures (up to ~70/day, with intermittent status epilepticus), which were confirmed via EEG and refractory to treatment with levetiracetam, clobazam, and phenobarbital. Additional signs included dyserythropoietic anaemia. Whole-exome sequencing identified compound heterozygous variants in CAD, consistent with a diagnosis of CAD deficiency: NM_004341.5:c.5441del (p.Gln1814Argfs*17), a novel pathogenic variant, and NM_004341.5:c.5428C>T (p.Arg1810Trp), a previously reported variant of unknown significance.

Management: Administration of uridine monophosphate was commenced two days post-diagnosis and led to a dramatic reduction in seizures, completely abolished status epilepticus, and improved alertness within days.

Conclusions: This case report expands the clinical spectrum of CAD deficiency three-fold: (1) It describes neonatal-onset CAD deficiency, contrasting reports of later-onset disease during infancy and childhood; (2) It adds extensive MRI head abnormalities to the repertoire of presenting signs; (3) It confirms uridine monophosphate as an effective treatment in neonates. Moreover, we report a novel compound heterozygous genotype observed in neonatal-onset CAD deficiency. An increased understanding of CAD deficiency is hoped to facilitate early detection and treatment of this neurometabolic condition.

Poster 131

Clinical spectrum of biallelic HPDL variants in childhood: expanding the phenotype

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4-hydroxyphenylpyruvate dioxygenase-like protein (HPDL) is the mammalian paralogue of the aerobic cell enzyme involved in the

L-tyrosine catabolism. HPDL function is not fully known, but biallelic variants in its encoding gene have recently been associated with a wide clinical phenotype ranging from severe infantile-onset neurodegenerative disorders characterised by developmental delay, seizures and cortical atrophy to milder phenotypes with spastic paraplegia in the second decade of life. Here we describe 3 new paediatric cases with biallelic HPDL variants. A 12-y old male, presented aged 8 with signs of spastic paraparesis, muscular weakness and urinary incontinence. His symptoms progressed, he became wheelchair dependent and developed internuclear ophthalmoplegia. Cognitive performances remained unchanged. 3 years after the initial presentation, his MRI showed new bilateral symmetric signal changes in the thalami and the anterior medulla, with cystic changes in the medullary olives. A targeted analysis of the HPDL gene confirmed compound heterozygous loss of function variants. The second and third case are siblings with a homozygous HPDL variant. The oldest sibling presented at 7 years of age with progressive spastic paraparesis with normal MRI brain scan. Over the following years she developed progressive muscle weakness, lower limb spasticity, urgency of micturition and became wheelchair dependent. Repeat brain scan at 13 years showed signal abnormality in the posterior aspects of the lentiform, medial thalamic and inferior olivary nuclei. Her younger brother presented a more severe clinical picture with global developmental delay and an emerging 4-limb spastic-dystonic motor disorder in the first months of life. Brain scan on day 6 showed underdevelopment of the frontal and temporal lobes, global delay in myelination with abnormal signal in the hilum of the dentate nucleus. These cases expand the radiological phenotype associated with HPDL and demonstrate previously unreported intra-familial variability in presentation.

Poster 132

TWNK biallelic mutations: a rare mitochondrial cytopathy manifesting with regressive encephalopathy, seizures and hyperkinetic movement disorders

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Objective: Mitochondrial disorders due to nuclear gene mutations present with multisystemic, predominantly neurological, manifestations. Due to their rarity and heterogeneity, presentations are often under-recognised. Despite the lack of curative treatments, clinical awareness and timely diagnosis is paramount to facilitate appropriate prognostication, counselling and management. Here, we describe such a case caused by biallelic TWNK mutations, expanding the phenotypic spectrum of the condition and reviewing the available literature.
Methods: Case study, detailing history of presentation, clinical examination, neuroimaging, electrophysiology, laboratory and genetic investigations.
Results: A white female with mild pre-existing neurodevelopmental delay presented at 13 months with a protracted illness manifesting as gastrointestinal upset, motor and cognitive regression. New onset choreoathetoid movement disorder evolved after the acute phase, as well as truncal ataxia and acquired microcephaly. Thorough investigations, including neurometabolic screen, EEG, MRI, muscle biopsy and targeted genetic testing (e.g. MECP2) were unremarkable. Whole exome sequencing was not performed due to suboptimal sample quality. A second distinct phase of regression at 14 years, consisting of encephalopathy, seizures and worsening of movement disorder, gut dysmotility, dysphagia and absent deep tendon reflexes. Liver investigations were essentially unremarkable. EEGs showed generalised encephalopathy with multifocal seizures. MRI showed evolving and fluctuating patchy bihemispheric cortical changes, cerebellar atrophy with signal change, spinal cord thinning, mild generalised brain volume loss and an elevated lactate peak on MR spectroscopy. Rapid trio exome sequencing revealed compound heterozygous likely pathogenic TWNK missense variants: maternally inherited c.1267A>T; p.(Thr423Ser) and paternally inherited c.1523A>G; p.(Tyr508Cys).
Conclusions: Our study expands the phenotypic spectrum of TWNK-related disorders, highlighting the co-manifestation of seizures and non-epileptic hyperkinetic movements often seen in mitochondrial cytopathies. It also emphasises the utility of next generation sequencing, and its role in providing a rapid, efficient, cost-effective way of determining the underlying aetiology of complex neurological presentations.

Poster 133

Neuropsychological profile of milder phenotypes of GLUT-1DS: a case series

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Objective: We aim to further characterise the neuropsychological function of children with a milder phenotype of GLUT-1, detailing neurocognitive ability and functional outcomes on serial assessments through childhood and adolescence.
Methods: This case series included children with non-classical form of GLUT-1DS referred for neuropsychological assessment at the John Radcliffe Hospital, Oxford between 1998 and 2019. All children were subjected to a range of neurocognitive assessments assessing intellectual ability, processing speed, attention, working memory, language, visuospatial skills, and academic abilities. Their scores on formal neurocognitive measures were converted to standardised scores to aid comparisons. In addition, parents completed standardised questionnaires about their child's behavioural and emotional functioning.
Psychosocial function was measured using the parent-completed version of the Strengths and Difficulties Questionnaire.
Results: Four children were available for analysis. Mean age of presentation was 6 years and presenting clinical features were absence epilepsy and paroxysmal kinesigenic dyskinesia.
All children attended mainstream school either with low (2) or high (2) level support.
All children had at least 2 neuropsychological assessments and time between first and most recent assessment had an average of 5 years (range 29–84 months). Intellectual abilities were 'low average' to 'very low' and over follow up, performance intelligence was more affected than verbal intelligence (VIQ 77–89, PIQ 67–81). All children had impaired visuospatial skills. Numeracy skills

were selectively impaired relative to literacy attainments (reading and spelling). Parents reported a high level of behavioural, social and emotional difficulties in all four children.
Conclusions: Neuropsychological profiles were suggestive of non-verbal learning difficulties, characterised by VIQ & PIQ, impaired visuospatial skills, selectively weak numerical skills and increased social, emotional and behavioural difficulties. We raise awareness of the need for general/community paediatricians to offer follow up for children with the non-classical form of GLUT-1DS to monitor learning difficulties/additional educational needs, particularly into and during secondary school.

Poster 134

[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.]

Abnormal tone and movements in an 8-month old infant

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Poster 135

Homozygous variant in NT5C2 gene associated with spastic diplegia, intellectual disability, periventricular white matter changes and thin corpus callosum.

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Background: Recent advances in genomic sequencing have identified genetic aetiologies for a proportion of patients who were previously characterised as having Cerebral palsy. NT5C2 (cytosolic 5^{i} -nucleotidase) gene mutations cause recessive forms of complicated hereditary spastic paraplegias (HSP). The protein plays a key role in both purine and pyrimidine nucleotide metabolism. Brain imaging findings of periventricular white matter changes and thin corpus callosum are reported in variants of spastic paraplegias adding further complexity to this already heterogeneous group of diseases.
Method: We present two siblings with similar clinical presentations of early onset lower limb spasticity and global developmental impairment. Our index case is now a 7-years-old male child born to consanguineous parents with an unremarkable perinatal history. He made some developmental progress, but does not have independent mobility and has moderate learning disability. His older female sibling had a diagnosis of cerebral palsy but also had a similar presentation in infancy. Other family members had varying degrees of learning disabilities and subtle motor skills issues. We investigated the male sibling extensively in view of the above history.
Results: Neuro-metabolic tests were normal. MRI brain scan noted marked bilateral periventricular white matter changes with volume loss, small cystic spaces surrounding the trigone and thin corpus callosum. His female sibling had similar MRI brain findings of widespread abnormalities in the white matter posteriorly, with some involvement of the corpus callosum. Sequencing analysis of DNA from the male detected a homozygous likely pathogenic variant in the NT5C2 gene: c.427C>T p.(Gln143Ter) which was also detected in his sibling.
Conclusion: With the presentation of these cases, we hope to contribute to the growing body of evidence detailing the clinical phenotypes of HSPs associated with gene defects in nucleotide metabolism.
Acknowledgements: Department of Molecular Genetics, Belfast City Hospital Trust, Belfast, UK

Poster 136

KBG syndrome associated with myoclonic absences - A case report

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Background: KBG syndrome (OMIM 148050) is a rare autosomal dominant syndrome first described in 1975, and is characterized by specific neurobehavioral, dental, craniofacial and skeletal anomalies, short stature and epilepsy. There is no report on the type of epilepsy that the children may have with this syndrome. We describe a case with myoclonic absences.
Case Description:
A 3 year old presented with the main concerns of developmental delay and epilepsy. The chromosome Microarray test had identified the 16q24.3 microdeletion. This involved partial deletion of the ANKRD11 gene which causes KBG syndrome. Our patient has dysmorphic features in keeping with KBG syndrome with unusual bushy eyebrows, a long upper lip with a well-formed cupid's bow and macrodontia of the incisor teeth. He has a single palmar crease on the left hand and mild clinodactyly. Our patient had epilepsy which started at around 3 years of age and mainly consisted of myoclonic absences. Seizures were difficult to control despite many anti-epileptic drugs and he underwent video EEG. Electro-clinical corelation of his typical seizures confirmed Myoclonic absence epilepsy. He continues to have 10–30 seizures per day despite being on Lamotrigine, Clobazam and Zonisamide. MRI Brain shows no focal lesion. Ketogenic diet and VNS are being considered. He also can have obsessions and tendency to aggressive outbursts.
Discussion: KBG is a very rare syndrome and only 400 cases worldwide have been identified. We highlight this case with KBG syndrome who has drug resistant myoclonic absence epilepsy as this association has not been described before. The case also illustrates the importance of genetic testing in providing diagnosis and better understanding to support the affected children and their families.

Poster 137

Phenotyping SFXN4 gene variants

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SFXN4 is a mitochondrially encoded protein involved in Iron-Sulphur cluster formation, Iron metabolism, intracellular Iron

distribution and heme synthesis. Reports of SFXN4 gene mutations are rare and describe a wide variety of symptoms. Here, we compared 6 patients to identify the phenotypic spectrum of SFXN4 variants. From this comparison, we have identified that patients are likely to present with intrauterine growth restriction, visual impairments and intellectual disability. They are also likely to have microcephaly. Further study of this rare genetic condition is required to fully understand its clinical presentation so as to assist identification and advise management.

Poster 138

Infantile onset biotin-thiamine-responsive basal ganglia disorder: A treatable condition to consider in acute onset encephalopathy with abnormal basal ganglia

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Objective: Biotin-thiamine-responsive basal ganglia disorder (BTRBG) is an extremely rare autosomal recessive disorder caused by mutation in the SLC19A3(solute carrier family 19, member3) which in early childhood presents with acute/subacute encephalopathy, seizures and movement disorder. We present a case of infantile onset BTRBG.
Case Report: A female infant born to non-consanguineous parents, presented at 6 weeks of age with encephalopathy and seizures. Full septic screen was negative for infection. Lactate was initially raised but remainder of the baseline metabolic investigations were normal. CT Brain showed low density in the posterior frontal, parietal and occipital lobes, lentiform nuclei and dentate nuclei. MRI Brain showed extensive symmetrical swelling and T2 hyperintensity in the posterior frontal, parietal and occipital lobes, lentiform nuclei, central midbrain, central pons and dentate nuclei with restricted diffusion in most of the areas. Trio exome sequencing identified compound heterozygous mutation in the SLC19A3 gene. Treatment was initiated with high dose biotin and thiamine. Despite treatment she has been left with significant sequelae including poor visual behaviour, central hypotonia, dystonia and epilepsy.
Conclusion: Biotin-thiamine-responsive basal ganglia disorder should be suspected in infants and children presenting with acute encephalopathy, dystonia and or seizures who have typical MRI changes including T2 hyperintensity involving universally basal ganglia, and in most cases thalami, cortical/subcortical areas, dentate nuclei and brain stem. Restriction diffusion in the affected areas and lactate peak on MRS can be seen. BTRBG also needs to be considered as a differential diagnosis in suspected Leigh's syndrome due to the similarities in clinical presentation, basal ganglia involvement and raised lactate. As early initiation of dual therapy with high dose biotin and thiamine can improve neurological outcome, we recommend initiation in all suspected cases whilst awaiting genetic results. Despite treatment infantile onset BTRBG is often more severe and is associated with a poorer prognosis.

Poster 139

Rare case of congenital disorder of glycosylation with RFT1 gene mutation presenting in neonatal period with apnoeic episodes

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A 1-month-old female was referred with several episodes of apnoea since the age of two weeks. She was born at term, mum had history of recurrent previous miscarriages. Noted to have dysmorphic features at birth including midface crowding, Hypertelorism, retrognathia, micrognathia, deep set eyes, low set ears with posterior slant, nuchal fold, overlapping clenched fingers and toes, adducted thumbs, contracture of left second index finger, singles palmar crease, inverted nipples. Mild contractures in both knees and left elbow, limited hips abduction, increased fat pad over both heals and right upper limb- hypotonia, other limbs stiff due to contractures. Had difficulties feeding and reflux, then developed apnoea and desaturation related to feeds. Seizures noted as recurrent brief slow tonic abduction of her upper limbs, with extension and stiffening of her lower limbs, abnormal jerky eye movements and head turning to side. Echocardiography, ultrasound abdomen, basic blood tests, metabolic tests workup and chromosomal microarray were normal. EEG showed abnormal background with frequent focal tonic seizures. MRI head showed partial agenesis of corpus collosum. Given her constellation of clinical features, genetic/metabolic cause was highly suspected and whole exome trio revealed homozygous mutation in RFT1 gene in chromosome 3p21.1, associated with congenital disorder of glycosylation (CDG) type 1n.
Discussion: CDG are a group of rare metabolic disorders with more than 130 subtypes, RFT1 gene encodes an enzyme that work in the pathway for the N-glycosylation of proteins. RFT1-CDG is a multi-system disorder, common features include developmental delay, hypotonia, visual/hearing defects, seizures, feeding difficulties, inverted nipples and dysmorphic features. To our knowledge only 10 cases of RFT1-CDG are reported in literature, mostly children and carry a very poor prognosis. Images will be shared on the presentation. We present this case to highlight the recognition of a very rare case which can present early on in neonatal period with apnoea and desaturation and this to be considered as a rare differential diagnosis.

Poster 140

The psychological impact of sudden traumatic bereavement causes metabolic decompensation in sisters with maple syrup urine disease

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Background: Maple syrup urine disease (MSUD) is a defect of the branched-chain alpha-ketoacid dehydrogenase complex, which is responsible for the breakdown of branched-chain amino acids (BCAAs) leucine, isoleucine and valine. Treatment includes dietary restriction of BCAAs, with good outcomes if management is initiated early. The aim is to describe a sibship pair, members of the travelling community, diagnosed with MSUD on newborn

screening; who experienced severe metabolic decompensation in the aftermath of the death of a much loved young relative.
Methods: We describe the clinical course of sibling X and sibling Y who both had an inpatient admission in the week following a traumatic bereavement.
Results: Sibling X, age 10, was admitted following a few episodes of vomiting at home. Her clinical examination was normal with no signs of infection. Her leucine level was elevated at 1381. Sibling Y, age 14, presented to the department two days after sibling X. She initially presented as a social admission, but on arrival had one vomit. Amino acid bloods were sent, but while awaiting these results her routine leucine level from the previous day was reported as 1022. Both siblings were managed with their unwell regimen – zero exchanges, 120% maintenance fluids and 20% lipid infusion. Both levels corrected to normal within three days.
Conclusion: Sibling X presented to the hospital three days after the death of their cousin in a road traffic accident. Sibling Y presented the evening of his funeral. Family and nomadism are core features of culture in the travelling community and this event posed significant stress on a tight-knit family. This case outlines two patients with a complex metabolic condition and displays the important connection between physical and emotional well-being. Both patients presented with a destabilised chronic illness despite full compliance to treatment and the absence of intercurrent illnesses.

Poster 141
Chromosome 15q13.3 deletion: A comparison of two cases

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Objective: We compare the clinical features of two cases of chromosome 15q13.3 microdeletion.
Case study: Case 1: 15-year-old male was referred to community team at 7 years of age for clumsiness, learning difficulties, constipation, overweight, mild speech delay and history of delayed walking. He developed absence seizures at around 8 years of age. Genetics study showed maternally inherited chromosome 15q13.3 microdeletion. MRI brain was normal. Autistic traits were noted by 11 years of age. He developed non convulsive seizures by 9 years and GTCS by 14 years of age. His seizure frequency has increased in spite of various anti-convulsants. Case 2: 17-year-old female presented at 8 years of age with absence seizures and idiopathic generalised epilepsy. She initially had good response to sodium valproate. At 13–14 years, she developed prolonged absence seizures and prolonged non convulsive seizures. She was diagnosed with chromosome 15q13.3 microdeletion around same time. Her parents did not have the microdeletion. MRI brain was normal. She only had mild learning difficulties but was doing well at school. She had GTCS and myoclonic status at around 15 years of age.
Discussion: Multiple neurological and psychiatric disorders have been identified with deletions of 15q13.3 but the syndrome itself remains ill-defined.1 Through this poster we have attempted to compare the clinical features of two children who have been diagnosed with chromosome 15q13.3 microdeletion and have been followed up at a district general hospital in east of England since birth. The aim is to contribute to the literature which might help in delineating the 15q13.3 deletion phenotype.

Poster 142
Health-related quality of life in children with neurocutaneous disorders

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Objectives: Health-Related Quality of Life (HRQoL) is an increasingly important clinical tool to guide patient management. Neurocutaneous Disorders (NCS) are a heterogenous group of genetic diseases affecting children and adolescents in different ways. The primary objective of this investigation was to assess quantity and quality of existing literature on HRQoL of children in NCS. Secondarily, recurrent themes that inform clinical management were identified.
Methods: A systematic literature review of MedLine via PubMed was performed for 41 different NCS. Neurofibromatosis and Tuberous Sclerosis were excluded from abstract screening (due to comprehensive HRQoL papers already identified and available). Recent systematic reviews aided further assessment. Ehlers-Danlos was excluded due to controversy regarding diagnoses and Fabry Disease was excluded due to its overlap status as a lysosomal storage disease.
Results: Initial search returned 796 papers on HRQoL across 41 syndromes. Following abstract screening and exclusion, 20 papers were identified across 9 diseases: Sturge-Weber Syndrome, Incontinentia Pigmenti, Klippel-Trenaunay Syndrome, Hereditary Haemorrhagic Telangiectasia, von Hippel-Lindau, Naevoid Basal Cell Carcinoma, Xeroderma Pigmentosum, McCune-Albright and Sjogren-Larsson Syndromes, addition to the comprehensive papers on Neurofibromatosis 1 and Tuberous Sclerosis.
Conclusions: The available literature on HRQoL in children with NCS is variable, with a shortage of research in some and an inconsistent approach in others. Recurrent themes included: (1) HRQoL is negatively affected in a variety of ways in children with NCS; (2) the psychological domain has particular significance, with recurrent focus on pain, anxiety and depression, and (3) varied syndromic phenotype is reflected in HRQoL. Limitations were identified and divided into inherent (e.g. heterogeneity of syndromes) and resolvable (e.g. inconsistent use of a standard HRQoL tool). Tentative conclusions can be drawn from the few syndromes with reliable evidence, notably Tuberous Sclerosis and Neurofibromatosis 1.

Poster 143
Development of a UK phase-2 clinical trial of 4'-phosphopantetheine for pantothenate kinase associated neurodegeneration

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Background: Pantothenate kinase-associated neurodegeneration (PKAN), a Neurodegeneration with Brain Iron Accumulation (NBIA) disorder, is an inborn error of vitamin B5-coenzyme A

(CoA) metabolism caused by biallelic mutations in the PANK2 gene. Children with classic PKAN present at a mean age of 3.4 years, often with gait difficulties and clumsiness; the atypical form presents later in adolescence or early adult life and progresses more slowly. PKAN is characterized by a severe movement disorder, cognitive and neuropsychiatric involvement, and pathological iron accumulation in the basal ganglia; these cause profound disability and risk of premature mortality. There are no proven disease-modifying treatments for PKAN.

Proposed therapy: PKAN is caused by functional loss of the mitochondrially-located PANK2 enzyme which phosphorylates vitamin B5 (pantothenate) in the first step of CoA metabolism. CoA is essential for the tri-carboxylic acid cycle, fatty acid oxidation and synthesis, amino acid metabolism and neurotransmitter synthesis, serving more than 9% of mammalian biochemical reactions. 4'-phosphopantetheine (4'-PPT) is the endogenous precursor to CoA and is found in all cells and many foods. In cultured human cells and the Pank2-knock out mouse model, administration of 4'-PPT corrects disease-specific phenotypes and does not cause toxicity.

Trial design: We will undertake a phase-2 clinical trial of enteral 4'-PPT administered once per day to 24 participants aged 1–25 years. A 6-month placebo-controlled, double-blinded, dose-ranging phase will be followed by an 18-month open-label, single-dose phase. Primary outcome measures are of safety and tolerability with regular blood test and side effect monitoring. The secondary outcome is response to treatment of a blood biomarker measuring the expression of CoASY mRNA, the last enzyme in the CoA synthesis pathway. Exploratory tertiary outcomes include questionnaire and examination-based disease rating scales, activity of daily living scales, measures of dystonia and quality of life, and functional ophthalmological assessments.

Poster 144

[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.]

A girl with gait difficulties

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Poster 145

Early features on MRI brain in neonatal myoclonic epilepsy supporting nonketotic hyperglycinemia

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Introduction: The elevated levels of glycine in the brain and CSF in Nonketotic hyperglycinaemia (NKH) cause neurologic impairment, which often presents early in life with neonatal encephalopathy. MR spectroscopy with glycine peak is the most characteristic radiological finding. We present another sign involving Posterior limb of internal capsule (PLIC) which is less known in NKH.

Case Report: A female neonate born at term by vaginal delivery with history of meconium aspiration and was treated with intravenous antibiotics. At day five of life, presented with myoclonic and focal seizures. Her EEG showed frequent bursts of diffuse spikes and polyspikes. MRI brain T2 sequence showed high signal in the posterior limb of internal capsule (PLIC) suggesting unmyelinated PLIC (expected to be myelinated in term baby). Notably, there was symmetrical restricted diffusion affecting whole of the posterior limb of internal capsule and extending down to the central trigeminal tracts in the dorsal brainstem and magnetic resonance spectroscopy showed Glycine peak at 3.55ppm. Her CSF glycine levels were elevated. She later received a confirmed genetic diagnosis of AMTC230C>TP mutation in the NKH gene.

Discussion and Conclusion: The most consistent abnormalities in NKH are noted on diffusion-weighted imaging in the first three months of life, when most individuals present clinically. The sites of abnormal signal intensity are confined to the white matter tracts that are myelinated at birth. High-signal-intensity DWI together with low apparent diffusion coefficient (ADC) probably reflect the well-known neuropathologic finding of vacuolating myelinopathy in NKH. Characteristic diffusion restriction in PLIC and tegmental tracts in the dorsal brainstem are a useful adjunct towards initial work up for possible NKH.

Poster 146

CASK gene deletion with microcephaly, intellectual disability and cerebellar vermis hypoplasia

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Objectives: Loss of function mutations of X-linked gene CASK (Calcium/calmodulin-dependent serine protein kinase) have been associated with intellectual disability and microcephaly with pontine and cerebellar hypoplasia (MICPCH) especially in females. The CASK gene (Xp11.4) encodes a member of the MAGUK (membrane associated guanylate kinase) protein family. It is highly expressed in the mammalian nervous system with possible roles in neurodevelopment and synaptic function. Complete loss of this gene is lethal in males. Affected persons may have normal OFC at birth, but develop progressive microcephaly, spasticity, dystonia and stereotypies of hand. Feeding, vision and hearing problems, epilepsy and minor dysmorphic features such as a protruding maxilla and maxillar incisors are also reported. There are only less than 50 cases reported worldwide.

Method: A 4 year old female child, born to non-consanguineous parents with unremarkable perinatal history presented with significant growth faltering and developmental impairment before 6 months of age. She had microcephaly, central hypotonia and had subtle dysmorphic features including arched eyebrows and a large nasal bridge. She had abnormal stereotypical movements of her hands and severe learning disability. She is awaiting a gastrostomy placement because of her feeding difficulties.

Results: Neuro-metabolic tests were normal. Array CGH analysis of DNA from the child identified an X chromosome microdeletion (Xp11.4p11.3). Analysis of parental samples showed this mutation was de novo. MRI brain scan at 20 months of age revealed hypoplasia of cerebellar vermis.

Conclusions: The clinical phenotype of our case is in keeping with those features described in the limited literature on CASK gene aberrations. Identification of such novel genes associated with MICPCH has provided new insights into the understanding of these disorders. Precise molecular diagnosis allowed targeted early interventions and genetic counselling of family.
Acknowledgements: Department of Molecular Genetics, Belfast City Hospital Trust, Belfast, UK

Poster 147

A gain-of-function mutation in CaSR gene caused hypocalcemia – a rare cause of recurrent seizures

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Objective: To report a rare hereditary endocrine cause of recurrent symptomatic seizures in a family.
Case Report: We report a family of two sisters and their father in whom the diagnosis of hereditary hypoparathyroidism remained elusive for a long time. A 6-year-old female attended an emergency department with a generalised convulsive seizure. Her birth history and development were unremarkable. Family history was remarkable for a sister having a diagnosis of epilepsy. Neurological examination was normal. Laboratory investigations revealed hypocalcemia, hyperphosphatemia, and low Parathyroid hormone. CT scan showed characteristic calcification. Similar findings were detected in sister (treated as epilepsy). Father who was asymptomatic showed similar metabolic/endocrine derangements. CaSR and PTH gene sequencing revealed Pro221Leu missense mutation in exon 3 of the CaSR gene in all affected family members. A final diagnosis of Autosomal Dominant Hypocalcemia (Gain-of-function mutation in the CaSR gene) was made.
Discussion: Familial isolated hypoparathyroidism is a group of rare genetic disorders characterized by decreased production of parathyroid hormone to maintain normal mineral balance. Parathyroid hormone plays a vital role in regulating calcium, magnesium, and phosphorus in the blood. Parathyroid hormone deficiency leads to hypocalcaemia and high levels of phosphorous. Familial isolated hypoparathyroidism is caused by changes in one of several different genes. The first symptoms usually appear in infancy, childhood, or young adulthood.
Conclusion: Advances in genetic diagnosis have changed medical practice.

Poster 148

[THIS POSTER HAS BEEN WITHDRAWN.]

Poster 149

Neonatal EEG features in Pallister Killian syndrome

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Objective: To describe the earliest electrographic features of Pallister Killian Syndrome in two infants.
Methods: Both infants had continuous video EEG monitoring using a modified neonatal montage. Genetic testing was performed via Comparative genomic hybridization microarray analysis.
Results: We describe two cases of PKS with distinctive electrographic features. Both infants had dysmorphic features including a combination of coarse flat facies, ante-verted nares, microphthalmia, high arched palate, low set ears, micrognathia and a large open fontanelle on the background of antenatal ventriculomegaly. Both experienced neonatal hypoglycaemia and had congenital abnormalities including cardiac defects, hearing impairments and abnormal brain MRIs characterised by perisylvian polymicrogyria and abnormal corpus callosums.
Both had suspected clinical seizures characterised by generalised limb jerking and myoclonic jerks respectively. Abnormal background EEG patterns were evident in both. Sleep wake cycling was present but quiet sleep phases were characterised by dysynchrony with long periods of suppression and excess of delta activity in case two. Three electrographic seizures were recorded in case one, consisting of sharp and slow wave complexes with onset in the left or right central regions with secondary generalisation which were treated successfully with 20 mg/kg of Phenobarbitone. In case two, myoclonic jerks were coincident with bursts of high amplitude movement activity in quiet sleep but no correlating electrographic seizures. Episodes ceased following a combination of Phenobarbitone and Levetiracetam. CGH microarray identified gains in the short arms of chromosome 12 at 12p13.33 to p11.1 in both cases consistent with a diagnosis of PKS.
At twelve months, case one developed refractory myoclonic seizures with global delay. Case two remains seizure free.
Conclusion: These cases, highlight the importance of early consideration of an underlying genetic disorder in infants presenting with highly abnormal background EEG patterns in the neonatal period.

Poster 150

Effectiveness of thymectomy in juvenile myasthenia gravis and clinical characteristics associated with better outcomes

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Objective: This review examines current evidence on the effectiveness of thymectomy in juvenile myasthenia gravis (JMG) and discusses clinical characteristics which may be associated with improved outcomes. Thymectomy is an established treatment in adult myasthenia gravis, but its exact role in JMG is still uncertain. Thymectomy is frequently considered in the treatment of severe, medically refractory JMG. Surgical approaches have evolved from open median sternotomy to the more cosmesis-preserving thoracoscopic approach.
Methods: A database search was performed on PubMed and Google Scholar to identify articles relating to thymectomy and JMG. The population was patients with JMG who underwent thymectomy, with comparators being medical therapy or no thymectomy. Outcomes included improved clinical status. The impact of surgical method, timing of intervention, presence of antibodies and state of thymic tissue were additionally assessed.
Results: 17 retrospective studies including 588 patients who underwent thymectomy from 1997 to 2020 were found, which either

reported uncontrolled cohorts undergoing thymectomy, or compared cohorts undergoing different surgical approaches. No randomised trials were found. An improvement in clinical status or reduced requirement for medical therapy following thymectomy was seen in 453 patients (77%). Complete remission was seen in 40% (n=172/430), calculated from studies with available data. Thoracoscopic approaches may provide improved outcomes, fewer complications, and better cosmetic outcomes. Better surgical outcomes may be associated with early intervention, intervention after the onset of puberty, being acetylcholine receptor antibody positive, having more severe disease and the presence of hyperplastic thymic tissue.

Conclusions: Available literature on the effectiveness of thymectomy in JMG is limited to retrospective studies of small cohorts. Nonetheless, current evidence suggests a role for thymectomy in JMG patients, especially those with certain clinical characteristics.

Poster 151

Real-life experience of delivering gene therapy with Onasemnogene Abeparvovec (Zolgensma®) for children with spinal muscular atrophy (SMA) in the UK

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Objective: To describe the real-life experience of delivering gene therapy with Onasemnogene Abeparvovec (Zolgensma®) to children with SMA in the UK.

Methods: Review of all referrals to the National Multidisciplinary Team (NMDT) in England (& Wales), and of the clinical records of all patients included for Zolgensma® therapy in the UK.

Results: Over 30 Zolgensma® infusions in England (& Wales), 2 in Scotland and 1 in Northern Ireland have been delivered so far. Full datasets were available for 20/30 patients. Age range was 2–19 months, weight 5.46 to 10.2kg, and follow-up 2–14 weeks. All patients had difficulties with venous access, often requiring anaesthetist input. Fever (10/20) and vomiting (8/20) were seen in about half of the patients. Liver function tests were normal pre-infusion in most patients (17/20); 3 had mildly elevated baseline AST/ALT. Virtually all patients developed transient transaminitis post-infusion, typically involving mild to moderate AST elevation resolving by week 3 (n=12/20). 8 patients had either more pronounced or more prolonged transaminase elevations; there was good response to increasing the steroid dose where indicated (n=5), and liver US and coagulation studies were normal. No thrombotic microangiopathy noted. Platelet count was normal pre-infusion in all patients. Asymptomatic transient thrombocytopenia (lowest 39) occurred invariably, typically early in week 1 and resolving by week 2. Most baseline troponin-T were elevated (16/18). Transient asymptomatic Troponin-I elevations seen in 5 patients resolved without any interventions and were associated with no significant cardiac US abnormalities. There was some correlation between troponin-T/I levels where data were available (n=3). 19 patients remain clinically well post-infusion and one admitted with enterovirus infection. CHOP-INTEND scores improved by 2–10 points (4/4).

Conclusions: All patients have remained well with no severe side-effects. Those with significant transaminitis responded well to doubling prednisolone. CHOP-INTEND scores where available show improvement from baseline.

Poster 152

Preserved swallowing function in Infants who initiated nusinersen treatment in the presymptomatic stage of SMA: Results from the NURTURE study

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Objective: Patients with spinal muscular atrophy (SMA) Type I or II have high rates of impaired swallowing function. Nusinersen has shown significant and clinically meaningful efficacy on motor function and survival endpoints across a broad spectrum of SMA patients. Our objective was to assess swallowing function over time among presymptomatic patients with SMA receiving nusinersen in the NURTURE (NCT02386553) study.

Methods: NURTURE is an ongoing Phase 2, open-label study evaluating nusinersen in infants genetically diagnosed with SMA who initiated treatment before the onset of clinical symptoms. Swallowing function was assessed using the Parent Assessment of Swallowing Ability (PASA) questionnaire, administered at multiple time points starting >1 year after treatment initiation. PASA includes 33 questions on general feeding, drinking liquids, eating solid foods, and parental assessment of swallowing concerns over the previous 7 days.

Results: Twenty-five participants (15 with 2 SMN2 copies, 10 with 3 SMN2 copies) aged ≤6 weeks at first dose were enrolled and received intrathecal nusinersen 12mg. As of the 19 February 2020 interim data cut, all 25 participants were alive with a median (range) age at last visit of 3.8 (2.8–4.8) years. For most items related to general feeding, drinking liquids, and eating solid foods, participants were consistently rated, on average, as never to rarely experiencing difficulty. At each timepoint, all participants with 3

SMN2 copies and the majority with 2 SMN2 copies were identified as being exclusively mouth fed.
Conclusions: Longitudinal results of this extensive swallowing assessment show preserved swallowing ability in participants who received nusinersen in the presymptomatic stage of SMA, in contrast to natural history and expected nearly universal swallowing insufficiency. Swallowing function continues to be monitored in NURTURE to better understand the efficacy of nusinersen over a longer duration of follow-up.

Poster 153

Scientific rationale for a higher dose of nusinersen

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Objective: Pharmacokinetic (PK)/Pharmacodynamic (PD) modelling evaluated the relationship between nusinersen cerebrospinal fluid (CSF) exposure and changes in CHOP INTEND score using data from nusinersen-treated participants with spinal muscular atrophy (SMA) in the CS3A (NCT01839656) and ENDEAR (NCT02193074) studies.
Methods: In both studies, participants had symptomatic infantile-onset SMA, SMA symptom onset at age ≤6 months, and were age ≤7 months at screening. The dosing regimen in CS3A comprised 3 loading doses of 6mg or 12mg nusinersen (Days 1, 15, 85), and 12mg maintenance doses every 4 months starting on Day 253. The dosing regimen in ENDEAR comprised 4 loading doses of 12mg nusinersen (Days 1, 15, 29, 64) and maintenance doses every 4 months thereafter (Days 183, 302).
Results: PK/PD modelling indicates that higher nusinersen CSF exposure leads to greater efficacy, measured by change from baseline in CHOP INTEND score. A higher dose regimen, consisting of 2 loading doses of 50mg nusinersen (Days 1, 15) followed by 28mg maintenance doses every 4 months, was designed to obtain nusinersen exposures with the potential to lead to even higher efficacy than the 12mg dose. Population PK modeling predicts achievement of ~2-fold higher nusinersen CSF exposure and PK/PD modeling predicts a clinically meaningful increase in CHOP INTEND score with higher dose compared with 12mg nusinersen. Population PK modelling shows similar steady-state CSF nusinersen exposures across a large range of body weights.
Conclusions: PK/PD modelling indicates that higher nusinersen CSF exposure leads to greater efficacy and that higher dose nusinersen may lead to greater efficacy than the 12mg dose. Steady-state CSF nusinersen exposures are similar across a range of body weights. The ongoing phase 2/3 DEVOTE study (NCT04089566) is evaluating the clinical efficacy, safety/tolerability, and PK of the higher dose nusinersen regimen in 5q SMA.

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The RESTORE Registry: Comparative outcomes in patients with spinal muscular atrophy (SMA) in the United States identified by newborn screening (NBS) or clinical diagnosis

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Objective: We sought to better understand outcomes in US children with SMA identified by NBS/prenatal screening versus those diagnosed clinically.
Methods: RESTORE is an ongoing, prospective, multicentre, multinational, observational study of patients with SMA. We stratified patients with ≤2 SMN2 gene copies and ≥16 months of follow-up into two groups based on SMA identification: clinical diagnosis based on SMA symptoms or NBS/prenatal screening. We compared age at diagnosis, age at first treatment, time from diagnosis to first treatment, proportion receiving monotherapy versus >1 treatment, and motor function changes.
Results: As of May 23, 2021, 55 patients met analysis criteria (42 clinically diagnosed; 13 NBS/prenatal diagnosis). Two NBS patients had one copy of the SMN2 gene and all other patients had two copies of the SMN2 gene. For clinically diagnosed patients compared with NBS patients, mean age at diagnosis was 3.2 versus 0.8 months ($p<0.0001$); age at first treatment was 4.9 versus 1.7 months ($p<0.0001$); and time from diagnosis to initial treatment was 1.3 versus 1.2 months ($p=0.8099$ [nonsignificant]). A significantly greater percentage of clinically diagnosed patients received >1 SMA therapy compared with NBS patients (90.5% [n=38/42] vs. 53.9% [n=7/13], respectively; $p=0.0118$). CHOP INTEND increases of ≥4 points were observed for 75.0% (n=15/20) of clinically diagnosed patients and 83.3% (n=5/6) of patients identified by NBS. Patients identified via NBS consistently achieved motor milestones at younger ages compared with clinically diagnosed patients.
Conclusions: NBS for SMA is associated with significantly earlier diagnosis and intervention. Compared with those who were clinically diagnosed, patients identified by NBS consistently achieved motor milestones at earlier ages, and more consistently achieved CHOP INTEND increases of ≥4 points. A significantly greater percentage of clinically diagnosed patients received >1 SMA therapy.

Poster 155

Endocrine and bone monitoring in boys with Duchenne muscular dystrophy: A dual centre audit

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Objective: In 2020, UK wide guidance on endocrine monitoring for boys with Duchenne Muscular Dystrophy (DMD) was agreed based on international standards of care(2018), following extensive consultation via the project DMD Care UK (www.dmdcareuk.org). This two centre audit aims to assess the adherence to these standards.
Methods: All boys undergoing clinical care in two tertiary neuromuscular centres (Glasgow and Leeds) were included. Audit standards were that all boys: (1) Should be on vitamin D supplements; (2) Have annual vitamin D levels measured; (3) Have annual lateral thoracolumbar spine imaging to identify vertebral fractures; (4) Annual clinical examination of puberty if aged 12 years and older; (5) Access to hydrocortisone for use as injection, with severe illness if on steroid treatment.
Results: A total of 104 boys were included, with median (range) age of 11.2 (2.1, 17.4). 84/104 (81%) were on steroids. 32/104 (31%) were non-ambulant. 83/104 (80%) were on vitamin D supplements. 80/104 (77%) had vitamin D levels measured in 2019. 94/104 (90.4%) had vitamin D level checked in the preceding 12 months. 73/104 (70%) boys had lateral thoracolumbar spine imaging in 2019 and 76/104 (73%) had imaging in the preceding 12 months. 54/73 (74%) had vertebral body abnormalities. Clear use of terminology with the use of the word fracture was only included in 21/54 (39%) of the abnormal reports. 32/44 (73%) who were eligible had examination of puberty. 78/84 (93%) had an emergency steroid plan with access to hydrocortisone for injection.
Conclusion: This dual centre audit of endocrine monitoring in DMD showed varied adherence with the agreed standards of care. Achieving optimal vitamin D levels is essential to optimise bone health and further evaluation into frequency of monitoring is needed. Annual spine imaging allows early diagnosis of vertebral fracture but lack of clarity of current reports may lead to inconsistencies in management. Targets for each standard should now be agreed to audit care throughout the UK.

Poster 156

Effectiveness and safety of Onasemnogene Abeparvovec in older patients with spinal muscular atrophy (SMA): Real-world outcomes from the RESTORE registry

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Objective: Interventional trials of onasemnogene abeparvovec (OA) demonstrated safety and efficacy in patients <6 months of age. We aimed to describe real-world outcomes in patients with SMA aged ≥6 months at the time of OA infusion.
Methods: We evaluated patients aged ≥6 months receiving OA (regardless of treatment with other disease-modifying therapies) in RESTORE, an ongoing, prospective, multicentre, multinational, observational registry study of patients with SMA.
Results: As of May 23, 2021, RESTORE included 117 patients with SMA aged ≥6 months at OA infusion (51 [43.6%] were ≥6–<12 months; 57 [48.7%] were ≥12–<24 months; and 9 [7.7%] were ≥24 months). The majority of patients (n=73/117; 62.4%) had two copies of the SMN2 gene. Thirty-eight (32.5%) patients received OA monotherapy; 26 (22.2%) were administered OA that was preceded and followed by nusinersen and/or risdiplam; and 53 (45.3%) patients switched from nusinersen to OA. Of 81 patients with information available, 41 (50.6%) weighed ≥8.5–13.5 kg at OA infusion. At infusion, the majority of patients (n=76/114; 66.7%) were diagnosed with SMA type 1; 7/114 (6.1%) were presymptomatic. Of 28 patients with ≥2 evaluable CHOP INTEND assessments, 25 (89.3%) increased or maintained score, and 18 (64.3%) achieved ≥4-point increases (11 patients aged ≥6–<12 months; 7 patients aged ≥12–<24 months). Adverse event (AE) data were reported for 116 patients; 71 (61.2%) reported at least 1 treatment-emergent AE; 33 (28.4%) reported at least 1 serious AE (20 [17.2%] related to OA treatment).
Conclusions: Patients with SMA aged ≥6 months at OA infusion benefited from treatment as measured by CHOP INTEND scores. The safety profile of OA in patients aged ≥6 months at infusion is consistent with the overall AE profile for OA, with no apparent pattern of AE incidence or severity according to age at infusion.

Poster 157

Nusinersen dosing patterns in patients with spinal muscular atrophy type 1 in the United States: Findings from a retrospective claims database analysis

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Objective: We sought to investigate dosing patterns and outcomes in patients with spinal muscular atrophy type 1 in the United States treated with nusinersen.
Methods: Using Symphony Health's Integrated Dataverse®, we identified patients diagnosed with SMA type 1 after nusinersen approval (Dec. 23, 2016) who initiated nusinersen and completed

the loading phase. Patients were followed until initiation of onasemnogene abeparvovec, last observed clinical activity or end of data availability (Nov. 30, 2019). Patients who received all doses on time (i.e., within seven days of the expected dosing date for loading doses and within 28 days for maintenance doses) were defined as adherent.
Results: Twenty-three patients with SMA type 1 received all four loading doses; 11 of 23 patients (47.8%) were adherent to the nusinersen dosing schedule, whereas 12 of 23 (52.2%) were non-adherent. SMA-related comorbidities were more prevalent in non-adherent patients compared with adherent patients. Eleven of 23 patients (47.8%) discontinued treatment (≥2 consecutive missed doses based on the expected dosing schedule). Median time to discontinuation was 18.5 months. At 12 and 24 months, 55.2% and 44.1% of patients, respectively, remained on treatment. No outstanding characteristics distinguished patients who discontinued or did not discontinue treatment.
Conclusions: These results indicate deviations from the recommended nusinersen dosing schedule, as well as prevalent treatment discontinuation, in real-world usage by patients with SMA type 1. Reasons for non-adherence can vary and may be related to logistical challenges for the patient or the patient's family, or the patient's health status on the day of planned treatment, resulting in a prolonged time period between injections. Treatment delays in these patients may result in loss of motor neuron function and disease progression.

Poster 158

Exploring the phenotypic variability of a large monocentric, paediatric cohort of non-ambulant patients with Duchenne muscular dystrophy

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Background: Boys with Duchenne muscular dystrophy (DMD) lose ambulation around 11 years of age, on average. While many clinical studies are available for ambulant patients, the non-ambulant phase of this condition is less well characterised.
Methods: Information was collected for all patients attending a newly developed tertiary non-ambulant DMD clinic between 10/2019 – 08/2021 at Great Ormond Street Hospital. We reviewed age at loss of ambulation (LOA), corticosteroid (CS) treatment and cardiorespiratory status. The Egen Klassification (EK) Functional scale and PUL 2.0 Upper Limb assessment were longitudinally performed in compliant children.
Results: At time of this review, 92 patients were seen at least once in the clinic. Age range at time of LOA was 6–16 years (mean 10.2 years, median 9.9 years). Mean (SD) age at first assessment was 13.7 (2.5) years), with a median of 2 visits per patient (max 4). At first evaluation, which happened at a mean (SD) age of 3.5 (2.6) years from LOA, EK scale and PUL2.0 were recorded in 89 and 47 patients with a median (IQR) value of 14 (10–19) and 25 (20–37.5). Twenty-seven individuals were not on CS; 31 were on prednisolone intermittent regimen, 12 on prednisolone daily, 12 on deflazacort intermittent, and 10 on deflazacort daily. The mean age at first visit of patients on CS vs naïve was 13.4 vs 14.6 years, respectively. There was a linear correlation between the EK and the PUL2.0 scale. No correlation between age at LOA and PUL2.0 or EK scale was observed.
Conclusion: Our data suggest a non-complete concordance between age at LOA and progression of weakness and function in the UL. Further correlation between CS use and genotypes are underway to shed insight on these findings.

Poster 159

Risdiplam for patients with spinal muscular atrophy in the United Kingdom under the early access to medicines scheme

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Objective: The first oral treatment for spinal muscular atrophy (SMA), known as risdiplam, was made available in the UK through the Early Access to Medicines Scheme (EAMS) between September 2020 and July 2021. Here we report the baseline characteristics and patient experience of enrolled paediatric patients (aged <18 years).
Methods: Eligible patients had a clinical diagnosis of Type 1 or 2 SMA, were aged ≥2 months and were not suitable for authorised treatments. Patient characteristics and risdiplam provision data were obtained from patients' treating physicians, and feedback was collected from patients and caregivers.
Results: Of the 241 patients enrolled in the scheme, 91 (37.8%) were aged <18 years, consisting of 43 males (47.3%) and 48 females (52.7%). The majority (84; 92.3%) of these patients were aged ≥6–<18 years, with four aged ≥2–<6 years (4.4%) and three aged ≥2 months–<2 years (3.3%). Fewer patients had Type 1 (19; 20.9%) compared with Type 2 SMA (72; 79.1%). Patients suffered from multiple co-morbidities, with scoliosis (69; 75.8%), previous spinal surgery (43; 47.3%), and ventilatory support (38; 41.8%) being the most frequently reported. In patients who had previously received a targeted SMA therapy (31; 34.1%), difficulties associated with intrathecal administration was the most reported reason for discontinuation. Most patients received risdiplam through Roche-funded homecare delivery (86; 94.5%) rather than hospital pharmacy collection (5; 5.5%).
Conclusions: Through the EAMS, risdiplam was made available to a substantial number of paediatric patients who were experiencing severe co-morbidities and were not suitable for any authorised SMA treatment. These findings demonstrate how access to innovative medicines via an EAMS can address significant unmet need for patients with rare diseases; though collection of longitudinal data for this complex population is recommended.

Poster 160

An audit on diagnostic pathways of paediatric hereditary motor sensory neuropathy in Northern Ireland

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Objective: To determine diagnostic pathways of Hereditary Motor Sensory Neuropathy (HMSN) in children, and identify opportunities to streamline services.

Methods: A retrospective audit was conducted on data collected from the Northern Ireland Electronic Care Record. Patients with a definitive diagnosis of HMSN confirmed by a positive gene panel before the age of 16 years were included. Primary outcomes were (i) Pathways to diagnosis, (ii) Mean age at diagnosis and (iii) Mean time from initial presentation to diagnosis.
Results: Services including physiotherapy, occupational therapy, orthopaedics, community paediatrics and paediatric neurology were commonly involved in the route to obtaining genetic confirmation of HMSN, however no consistent pathway between patients was identified. Mean age at diagnosis was 7.4±4.3 years. Mean time from initial presentation to diagnosis was 2.9±2.6 years. Electromyography and Nerve Conduction Studies were performed for 50% of patients prior to diagnosis, with a mean time of 11.75±8.66 months from order to results.
Conclusions: Observed diagnostic delays represent a need for dedicated guidance on diagnosis of HMSN in children to improve the efficiency and effectiveness of the pathway and achieve earlier, appropriate treatment.

Poster 161

Heterogeneity and overlap in childhood hereditary spastic paraplegias: A clinical review of six new cases

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Introduction: Hereditary spastic paraplegias (HSP) are a diverse group of gait disorders, caused by a distal neuropathy of the longest corticospinal tract axons which were usually misdiagnosed in the past with cerebral palsy. New genetic testing, such as Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS) have allowed an early diagnosis of this condition.
Material and Methods: We conducted a descriptive, retrospective study of 6 patients with a diagnosis of HSP followed up in our hospital. We describe the genetic, clinical and neuroradiology outcomes of these cases.
Results: We present 6 patients with a genetic diagnosis of HSP, four boys (66.7%) and two girls (33.3%). The mean age of the patients is 9.18 years ± 4,37 SDS (Range 4.7–17.5 years old). Family history was present in 4 cases (66.7%). Genetic testing identified mutations at the SPAST (HSP type 7), CYP7B1 (HSP type 5A, 2 siblings), SPAST (HSP type 4), CYP2UI (HSP 56) and REEP (HSP type 31) genes. Mean walking age was 15.33 months ± 4,63 SDS (Range 11–24 months old). Main motor symptoms were the presence of a progressive spastic diplegia (100%) with brisk reflexes in 4 patients (66.7%) associated with lumbar lordosis, 2 HSP 5A cases (33.3%) and equinus feet deformity, 2 cases, HSP 4 and HSP 56 types (33.3%). Two patients with HSP 5A presented bowel and bladder incontinence with macrocephaly. Brain MRI was performed in all patients, two patients presented an incidental finding of cerebellar ectopia (HSP 56) and hydromyelia (HSP 31) respectively. One patient associated a diagnosis of autism spectrum disorder (HSP 56).
Conclusions: WES and WGS techniques have helped identify several genes implicated in childhood HSP. This clinical review identifies the different phenotypes and illustrates the heterogeneity of this condition.

Poster 162

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

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Objective: SMA is a severe neuromuscular disease in which motor neuron degeneration may occur in the first months of life, often before symptoms appear. Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier approved by the FDA, EMA and MHRA for the treatment of patients with SMA, aged ≥2 months, with Types 1–3 SMA or with 1–4 SMN2 copies. RAINBOWFISH (NCT03779334) is a multicentre, open-label, single-arm study that investigates efficacy, safety and pharmacokinetics (PK)/pharmacodynamics of risdiplam in infants with genetically diagnosed presymptomatic SMA.
Methods: RAINBOWFISH is actively enrolling infants aged from birth to 6 weeks (at first dose), regardless of SMN2 copy number. Infants 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) amplitude ≥1.5 mV at baseline. The primary endpoint is the proportion of these infants sitting without support for ≥5 seconds at Month 12. Secondary endpoints include the development of clinically manifested SMA, survival and permanent ventilation, achievement of motor milestones, motor function, growth measures, nutritional status, CMAP, PK and safety monitoring.
Results: For the first 12 enrolled infants, the median age at first dose was 28.5 days (range: 16–40 days). We will report baseline demographics of enrolled infants with presymptomatic SMA. Preliminary efficacy and safety data in presymptomatic infants will also be presented.
Conclusions: RAINBOWFISH will provide valuable information about presymptomatic administration of risdiplam and will help determine the dose of risdiplam for infants <2 months of age. Recruitment is ongoing worldwide.
Acknowledgements: The authors would like to thank all individuals enrolled in the risdiplam studies, their families and the site staff involved. Study sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

Poster 163

Pooled safety data from the risdiplam clinical trial development program

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Objective: Spinal muscular atrophy (SMA) is a severe, progressive neuromuscular disease with a broad age range and spectrum of disease severity. Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier approved by the EMA and MHRA for the treatment of patients with SMA, aged ≥2 months, with Types 1–3 SMA or with 1–4 SMN2 copies. These pooled analyses investigated the safety of risdiplam across the clinical development program.
Methods: Safety data were pooled from three studies within the risdiplam clinical development program, covering a broad SMA population: (1) FIREFISH (NCT02913482) assesses safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and efficacy of risdiplam in infants with Type 1 SMA (aged 1–7 months at enrolment); (2) SUNFISH (NCT02908685) assesses safety, tolerability, PK, PD and efficacy of risdiplam in patients with Types 2/3 SMA (aged 2–25 years at enrolment); (3) JEWELFISH (NCT03032172) assesses safety, tolerability, PK and PD of risdiplam in patients with SMA (aged 6 months–60 years at enrolment) who previously received RG7800 (RO6885247), nusinersen (SPINRAZA®), olesoxime or onasemnogene abeparvovec (ZOLGENSMA®).
Results: Pooled analyses from FIREFISH, SUNFISH and JEWELFISH showed no treatment-related safety findings leading to withdrawal from risdiplam treatment for up to 38.9 months in 465 patients (data-cuts: 14 November 2019, 15 January 2020 and 31 January 2020, respectively). Differences in adverse event profiles between Type 1 and Types 2/3 SMA populations appeared to be driven by the severity of the underlying disease. Here we will present updated pooled safety analyses.
Conclusions: Pooled safety data across the risdiplam studies will add to the understanding of the long-term safety profile of risdiplam.
Acknowledgements: The authors would like to thank all individuals enrolled in the risdiplam studies, their families and the site staff involved. Study sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

Poster 164

Popeye arm and inverted axillary fold signs – clinical markers for facioscapulohumeral muscular dystrophy

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Objective: To underscore the importance of Popeye arm and inverted axillary fold signs as clinical markers to guide genetic testing for FSHD.
Case Report: An 8-year-old girl presented with progressive weakness of face and arms, with evolving gait difficulties. Her father with a similar - but milder phenotype had not received a diagnosis. Both showed a Popeye arm sign and inverted axillary fold signs. Their CK levels were mildly elevated. They showed myopathic pattern on EMG. Their genetic testing for FSHD confirmed the diagnosis.
Discussion: Facioscapulohumeral dystrophy (FSHD) is a rare neuromuscular disease which is characterized by progressive skeletal muscle weakness, especially the muscles of face, scapula and arms. FSHD is often asymmetrical. Symptoms may appear years before a formal diagnosis. In FSHD, the biceps and triceps are more severely affected while the deltoid and forearm muscles are relatively spared. The thinning of the arm with relatively normal bulk of the deltoid and forearm resembles the cartoon character, Popeye. The Popeye arm appearance (Popeye's arm sign) is highly specific for FSHD. In addition, there is characteristic prominence of axillary fold anteriorly, rather than posteriorly.
Conclusion: The clinical signs such as Popeye's arm sign and inverted axillary fold can be used as clinical markers for targeted genetic testing.

Poster 165

Perisylvian polymicrogyria and lower limb predominant SMA-like picture – joining the dots!

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Case Presentation: A four-year-old girl, with no significant family history, was detected to have ventriculomegaly on antenatal 20-week ultrasound. She presented at eight months of age with epileptic spasms. MRI brain revealed bilateral posterior perisylvian polymicrogyria with simplified cortical gyral pattern, suggestive of a diffuse neuronal migration disorder. Bilateral ankle and knee contractures became apparent in infancy. Arthrogryposis and orthopaedic foot deformities like rocker bottom feet were considered as differentials. Nerve conduction and electromyography studies revealed chronic neurogenic changes in at least three spinal levels and normal sensory study, pointing to either an anterior horn cell disorder or a motor axonal neuropathy. Subsequently, she developed epilepsy, which was medically managed with anti-seizure medication, with an option of offering ketogenic diet if it became drug resistant. The child was investigated for a probable genetic cause, for a unifying explanation of perisylvian polymicrogyria and bilateral lower limb contractures. Structural brain malformation gene panel revealed DYNC1H1 c.4867C>T heterozygous mutation, classified as pathogenic.
Discussion: DYNC1H1 encodes for a subunit of the cytoplasmic dynein complex which plays an important role in trafficking of

cellular cargo to the minus-end on microtubules, for spindle pole organization, Golgi maintenance, endolysosomal processing, and nuclear positioning migration during mitosis in eukaryotic cells. Typically, children with mutations in the DYNC1H1 gene have neuronal migrational disorders and perisylvian polymicrogyria. They may also present with an additional characteristic phenotype of lower limb predominant SMA-like picture with motor delay and lower limb contractures, due to involvement of anterior horn cells. It is also described as autosomal dominant lower limb extremity predominance spinal muscular atrophy or described as dominant Charcot-Marie-Tooth disease or hereditary motor sensory neuropathy type 2. Our case highlights perisylvian polymicrogyria and lower limb contractures due to motor neuron involvement as a distinct phenotype due to DYNC1H1 gene mutation.

Poster 166
Ears of Lynx: A distinct MRI sign in hereditary spastic paraplegia

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Introduction: We describe a 15-year-old patient presenting with spastic paraparesis in whom a distinct radiological sign steered investigation to clinch a diagnosis of HSP-11.
Case Report: A 15-year-old girl presented with altered gait since the age of twelve. On walking, she had mainly toe walking with a spastic gait and tight hamstrings and tendoachilles. It was noted in the clinic that mum had received a diagnosis of "fibromyalgia" and was walking with the aid of a walking cane. Her examination was consistent with spastic paraparesis with brisk deep tendon reflexes in child and mother. Her MRI showed Corpus callosum thinning and periventricular white matter signal abnormality near the frontal horns of lateral ventricle on axial T2. She was being treated as probable Dopa responsive dystonia for years before presentation. The clinical presentation bearing similarity in the young lady and her mother, with neuroimaging findings on formers MRI Brain led to the investigations to confirm HSP.A genetic analysis confirmed the diagnosis of autosomal recessive HSP type 11 clinching the diagnosis in the child and her mother.
Discussion: Thinning of the corpus callosum has been described as the most frequent abnormality in almost one-third of recessive HSPs. Focal thinning in the genu fibres of the corpus callosum with accompanying T2/FLAIR hyperintensity in the periventricular white matter abutting frontal horns of the lateral ventricle described as the "ears of the lynx" sign (Lynx is a medium sized wild cat with distinct hair tufts at the tip of its ears)and has been related to two recessive forms of HSP, type 11 and 15. In the diverse clinical context and without specific MRI findings, the ears of the lynx sign is an important sign which helps narrow the differentials in a presentation with spastic paraparesis.

Poster 167
JEWELFISH: Safety, pharmacodynamic and exploratory efficacy data in non-naïve patients with spinal muscular atrophy (SMA) receiving treatment with risdiplam

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Objective: SMA is a severe, progressive neuromuscular disease affecting a broad age group with a spectrum of disease severity. Risdiplam (EVRYSDI®) is a centrally and peripherally distributed, oral survival of motor neuron 2 (SMN2) pre-mRNA splicing modifier approved by the EMA and MHRA for the treatment of patients with SMA, aged ≥2 months, with Types 1–3 SMA or with 1–4 SMN2 copies.
The JEWELFISH study assesses safety, tolerability and the pharmacokinetic/pharmacodynamic (PD) relationship of risdiplam in non-treatment-naïve patients with SMA.
Methods: JEWELFISH (NCT03032172) is a multicentre, open-label study of daily risdiplam in patients with SMA aged 6 months–60 years who previously received RG7800 (RO6885247), nusinersen (SPINRAZA®), olesoxime or onasemnogene abeparvovec (ZOLGENSMA®).
Results: JEWELFISH (N=174) includes a broad range of ages (1–60 years), SMA types (1–3), SMN2 copy numbers (1–4) and motor function (non-sitters, sitters and walkers). We previously presented safety data from 173 patients (data-cut: 31 July 2020) who received risdiplam for up to 41 months. Risdiplam led to a rapid and sustained, >2-fold increase in SMN protein levels versus baseline (data-cut: 1 June 2020), which was consistent with data from the SUNFISH study of treatment-naïve patients with Types 2/3 SMA. No drug-related safety findings leading to withdrawal were reported for any patient in JEWELFISH. The safety profile of risdiplam was consistent with that observed in treatment-naïve patients. Here we present updated 12-month safety, PD and exploratory efficacy data.
Conclusions: JEWELFISH is ongoing at sites across Europe and the US and will provide important data on the safety, PD and exploratory efficacy of risdiplam in a broad population of non-naïve patients with SMA.
Acknowledgements: The authors would like to thank all individuals enrolled in the risdiplam studies, their families and the site staff involved. Study sponsored by F. Hoffmann-La Roche Ltd, Basel, Switzerland.

Poster 168

Paediatric arterial ischaemic stroke during the COVID-19 pandemic: a collaborative North of England study

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Background and Aims: SARS-CoV-2 as a possible cause for childhood arterial ischaemic stroke (AIS) has been described in a few case reports in literature. We sought to determine rates of AIS in paediatric patients across the North of England during a 12 month period, aiming to establish the underlying aetiology of their stroke.

Methods: Tertiary paediatric neurosciences centres across the North of England (Manchester, Liverpool, Sheffield, Leeds, Newcastle) collected retrospective data on patients with AIS and collated information on the following areas: patient's age at presentation, aetiology, co-morbidities, COVID-19 status, imaging modalities, hyperacute therapy and any further management carried out.

Results: From February 2020 to February 2021, 32 paediatric patients were diagnosed with AIS (age range 1 month-15 years, mean age 6.1 years). Aetiology consisted of idiopathic 29.1%, underlying vascular abnormality 25%, cardio-embolic 18.7%, post-operative complications 12.5%, coagulopathy 6.3%, infection 3.1%, and inflammatory/vasculitic 3.1%. At presentation and subsequent testing, 100% of patients were negative on COVID-19 PCR testing. Of note, one patient tested positive a month prior to admission, but negative on presentation and the stroke was not felt to be linked to COVID-19.

Conclusions: Analysis of our regional data did not demonstrate that SARS-CoV-2 caused an increase in the number of patients diagnosed with AIS. Although COVID-19 testing is recommended in all patients presenting with AIS, we should not attribute the AIS to COVID-19 unless all other causes have been excluded.

Poster 169

Paediatric acute ischemic stroke: Systematic review of diagnosis and management over the past three decades

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Similarities and differences exist between paediatric and adult populations in etiology, presentation and management of stroke. In children, stroke has numerous etiologies and predisposing risk factors along with a larger range of presenting symptoms and signs. As a result, accurate and timely diagnosis of stroke in paediatric populations is delayed worldwide. We performed a systematic review to evaluate clinical presentation, diagnosis and management of paediatric stroke cases between 1990 and 2021. 627 papers were identified on PubMed. 38 papers were included in the review and underwent data extraction, including information on 2,823 children. Children between 28-days and 18-years of age with acute ischaemic stroke were included in the study population. Information regarding population demographics, risk factors, prior diagnoses, signs and symptoms, time to presentation and imaging, types of imaging, national and international guidelines, treatments, and patient outcomes were extracted from papers. Only a third of papers referred to local or national guidelines on paediatric stroke. We found that infection and head and neck trauma were the most common acute risk factors (7.4% and 6.1% of the population respectively), with cardiac disease and vasculopathy the most common pre-existing conditions (28.4% and 19.9% of the population respectively). 39% of patients presented with hemiparesis. We were unable to identify significant differences in the time from symptom onset to initial imaging over time. Treatment varied, and thrombectomy and thrombolysis numbers were low with 1.4% and 0.2% of patients receiving the respective interventions. In summary we highlight that delays in management are primarily due to untimely identification of symptoms and diagnosis.

Poster 170

Diversity in a UK tertiary paediatric neurovascular service over a 5-year period

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Background and Aims: There is an expanding evidence base for advancing therapies applicable to pediatric neurovascular disorders which indicate that children are best served by a multidisciplinary team with a wide range of expertise. We sought to analyse the individual characteristics within our own patient cohort.

Methods: Analysis of patients referred to the service), over a period of 5 years (2016–2021) was carried out using an ongoing patient database. Data was collected concerning age, gender, diagnosis, rates of surgical intervention and sequelae of disease (including physical deficits, epilepsy, and developmental/cognitive complications).

Results: 117 patients were analysed across the 5 year period. The commonest active diagnoses consisted of cavernomas (n=27, 23.1%), arteriovenous malformations (n=22, 18.8%) and Moyamoya disease (n=18, 16.2%), many of which have an identifiable genetic basis. 37 patients (31.6%) were identified as having an underlying genetic diagnosis, the commonest being Neurofibromatosis type 1, Trisomy 21 and CCM gene mutations.

Conclusions: Approximately one third of our patient cohort were identified as having a genetic basis for their neurovascular disease, representing a significant proportion of the population. It is crucial that as advancements in the approach to paediatric neurovascular disease are made, that involvement of clinical genetics is sought in order to optimise the evaluation of neurovascular patients. The expertise and infrastructure gained over five years have enabled the service to work toward a vision of leading an acute pediatric stroke service in the North West.

Poster 171

Primary leptomeningeal ATRT mimicking stroke: A case report

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Introduction: Atypical Teratoid Rhabdoid Tumour (ATRT) is a rare paediatric CNS malignancy which typically occurs in children under three years of age and is characterised by its infratentorial location, rapid progression and relatively short symptomatic prodrome. We describe an exceedingly rare case of leptomeningeal ATRT presenting with radiological features initially suggestive of arterial ischaemic stroke.

Case: A previously well 8-year-old boy presented with sudden onset left sided weakness and prolonged left focal seizures requiring ventilation. CT brain revealed hyperdensity in the right middle cerebral arterial territory and MRI confirmed ischaemia on diffusion-weighed imaging. However, MR angiography was completely normal with no obvious vascular anomalies. The patient and made a rapid clinical recovery within a few days. Repeat MRI/MRA on day five remained unchanged. In view of these unusual findings, potential stroke mimics were considered. Baseline metabolic, inflammatory and autoimmune investigations were normal. The patient was discharged with a plan for repeat MRI with contrast in 8 weeks. However, he represented 5 weeks later with severe headache and vomiting. Urgent imaging revealed significant leptomeningeal enhancement. Brain biopsy confirmed primary diffuse leptomeningeal ATRT (WHO Grade IV). He commenced chemotherapy as per the EurHab protocol, with ongoing clinical and radiological surveillance.

Discussion: Primary diffuse leptomeningeal ATRT is very poorly described in literature. We have identified only one other reported case which described a 30-month-old child presenting with presumed leptoencephalitis but was later diagnosed with primary diffuse leptomeningeal ATRT. Our case is unique as the patient is outside the typical age range and initially had lacking radiological evidence of a solid tumour.

Conclusion: To our knowledge, this is only the second case reporting primary CNS ATRT involving the leptomeninges without the presence of an intraparenchymal mass. Early imaging with contrast is recommended when the clinical presentation does not completely fit with arterial ischaemic stroke.

Poster 172

A spectrum of vascular abnormalities in PHACES syndrome - a case series

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Objective: PHACES is a multiorgan syndrome consisting of Posterior fossa malformations, Haemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities and Sternal malformations. Vascular anomalies and abnormalities are a predominant clinical problem in PHACES syndrome. Our case series aims to demonstrate the spectrum of vascular abnormalities in PHACES.

Cases: Child A had an antenatal diagnosis of dandy walker syndrome and presented at birth with left facial haemangioma, craniofacial abnormalities, small optic nerve and ventriculoseptal defect. MRI showed complex malformation of the circle of Willis, persistence of embryonic vasculature and absence of normal internal cerebral veins and straight sinus. At five she developed acute hemiparesis secondary to a left gangliocapsular infarct. She subsequently experienced multiple transient ischaemic events. Angiogram showed complex malformations with both anastomoses and aneurysmal dilatation of the distal carotid artery consistent with moyamoya phenomenon. She underwent successful Encephaloduroarteriosynangiosis (EDAS) procedure. Child B presented with a large haemangioma of her left scalp and microcornea. Prenatal MRI suggested dandy walker syndrome. Postnatal MRI scans showed left cerebellar hypoplasia, left cerebral artery dysplasia and an atypical cavernous segment of the left internal carotid artery. At three years old she remains clinically asymptomatic. Child C presented with a left facial and scalp haemangioma and stridor as a neonate. Urgent micro laryngoscopy revealed a large haemangioma of the vocal cords and sub glottis requiring intubation. MRI showed multiple haemangiomas within the left orbit, face and a large haemangioma extending from the left skull base to the mediastinum surrounding the carotid, jugular and aortic arch. Medical treatment with propranolol caused significant reduction in size of the haemangiomas allowing extubation. She was discharged self ventilating in air with resolution of stridor.

Conclusion: PHACES incorporates a spectrum of vascular abnormalities both intracranial and extracranial of varying severity. Awareness about this can help provide appropriate neurovascular imaging surveillance.

Poster 173

A case report of Moyamoya disease with characteristic EEG and angiographic findings.

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8 years old girl referred by the GP to paediatric epilepsy clinic with complaints of having recurrent paroxysmal episodes following a tonsillitis like illness that lasted for 2 weeks. There were two different episodes with motor symptoms of arm weakness lasting for not more than 30 minutes. Other episodes included sensory symptoms like tingling sensation in the arms, fingers and tongue and an episode when speech was described to be slow but not slurred. Consciousness wasn't impaired and she made full recovery after the episodes. Later, during the course of her illness she also complained of headaches which were mild, not clinically suggestive of migraine headaches. Family history was insignificant. She was described as anxious child and these episodes made her more anxious. General and systemic exam including neurological examination was unremarkable. Differential diagnoses included focal epilepsy and migraine with aura. An awake EEG and MRI brain was done soon after the clinic visit. MRI brain was unremarkable and the awake EEG revealed abnormal persistent slowing following hyperventilation for 4 minutes with frontal predominance during which the patient was asymptomatic. Following the EEG report, an MRA was performed which

confirmed moyamoya pattern with severe stenotic appearance of bilateral MCA with relative lack of flow and presence of excessive collateralisation around the circle of Willis. A final diagnosis of transient ischaemic attacks secondary to Moyamoya disease was given to parents. She is now undergoing evaluation in paediatric neurology unit after a prolonged transient ischaemic attack.

Poster 174

Unusual case of paraparesis: Spinal metameric arterio-venous malformation treated with selective embolization

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A 10-year-old pre-morbidly normal girl presented with acute onset rapidly progressive paraplegia with sensory level and bladder and bowel incontinence. MRI spine showed a 5x5x7mm ovoid lesion within the central component of the spinal cord at the level of T6 with associated vascularity and multiple serpiginous vessels within the adjacent spinal canal. Subsequent MR angiogram of the spine demonstrated complex metameric arterio-venous malformation (AVM) involving the spinal cord, vertebral body and intercostal muscle at the level of T8-T9 with diffuse cord oedema and haemorrhage in the thoracic spine. Selective embolization of the feeder vessel was undertaken successfully in two stages which resulted in significant improvement in the appearance of the cord oedema and vascular malformation on repeat spinal MRA. The patient underwent intense neurorehabilitation and showed significant neurological improvement post the embolization procedure. Follow on MRI scan one year post embolization showed a small residual dorsal AVM which will be monitored with annual MRI scans. Spinal metameric arteriovenous malformations (AVM) are rare in children and remain underdiagnosed as a cause of myelopathy. They are characterized by an intradural and extradural component. These are malformations of non-hereditary metameric origin affecting not only the central nervous system but also other tissues originating from the same metamere. The vascular disorder can lead to recurrent haemorrhage and neurological deficits. Embolization of feeding vessels in metameric spinal AVMs can be technically challenging due to the risk of iatrogenic ischaemia but when successful can lead to a good outcome.

Poster 175

Introduction of an allied health professional led clinic for paediatric neuro oncology: A pilot within Southampton Children's Hospital

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Objectives and Background: Robbie's Rehab provides specialist neuro-rehabilitation for children diagnosed with brain and spinal tumours under the care of Southampton Children's Hospital. Having a brain tumour and its treatment can have a wide impact on a child and their families' quality of life and return to "normal life" with limited time to explore these within standard clinics. A pilot supplementary clinic to focus on these aspects was initiated by a physiotherapist, psychologist and nurse specialist, primarily reviewing non-medical concerns, supporting return to school and home life.
Methods: Review of Prospective data collected for patients attending the Robbie's Rehab Multidisciplinary clinic October 2020-February 2021.
Results: 22 patients were offered an appointment, 2 declined to attend. Due to COVID only 1 patient attended face to face, the remainder via Attend Anywhere video consultation. 16 patients had a diagnosis of a low grade tumour and 4 patients had high grade tumours. All patients had completed oncology treatment. 3 common areas of concern were identified by patients and parents; fatigue, educational difficulties and emotional difficulties. Advice and support was provided during clinic where appropriate and referrals to other services were made (play support, endocrine referral). Additional interventions occurred outside the clinic from the Robbie's Rehab Team (physio assessment, psychology support, cognitive assessment). Post clinic parental questionnaire completed by 18/20 families. 11/18 parents rated the clinic as helpful and 7/18 parents rated the clinic as extremely helpful. 100% would definitely recommend attending this clinic to other parents.
Conclusion: The addition of a quality of life focused MDT clinic run by members of the extended neurooncology team has been effective in improving the patient and parent experience of life after oncology treatment.

Poster 176

A 5 year review of the key worker role within Southampton children's integrated rehabilitation team (SCIRT)

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Objective: Review experiences of staff and families of key worker role, implemented to comply with NHSE service specification (specialised rehabilitation for patients with highly complex needs). "Services should use a key worker system, where each individual is allocated a named person as their main point of contact and communication with the rest of the team." "That there should be structured feedback of views from patients and family about all aspects of the service through questionnaires." SCIRT is a 4 bedded level 2A designated rehabilitation service, integrated within the tertiary neurology service. All families with an expected admission >2 weeks are assigned a key worker, and provided with feedback questionnaire at discharge.
Method: Discharge questionnaire Data (2016–2021) exploring family experience of key worker extrapolated. Qualitative questionnaire sent to current MDT for feedback of staff experiences analysed.
Results: 66 discharge questionnaires competed. 82% included key worker information. Of the 70% (n=46) that identified having a key worker 96% felt they met with their key worker enough, 0% stated too often and 4% not enough. 87% found key worker sessions completely helpful, 11% classifying generally helpful and

2% (n=1) not helpful. 7 responses to MDT staff questionnaire. All disciplines represented (n=6). Mean time spent per week on key worker role 95 minutes. Staff ranked the roles/responsibilities. Highest were: discussion of goals, meeting regularly with the families, liaison/communication between families and the wider team. 100% classified this role as important with 5/7 rating it vital. Only 28% felt extremely confident in undertaking this role. There was a high degree of variability on how sessions took place and documentation.
Conclusions: Key worker role is found to be beneficial by both families and staff , but has high demands on the clinical staff both regarding time pressures and complexity outside of usual scope of practice.

Poster 177

Disorders of the autonomic nervous system: experience of a paediatric neurology syncope clinic

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Objective: To review the referral pathway, case mix, and outcomes of children and young people referred to a paediatric neurology syncope clinic.
Method: A retrospective, observational, clinical notes review of consecutive cases referred over 2 years. A Clinical Global Impression (CGI) outcome assessment was made by one author not directly involved in the clinic, from the notes, where there was sufficient follow-up.
Results: 55/61 (90%) were referred for assessment of a possible disorder of the autonomic nervous system: 31/55 (56%) with transient loss of consciousness (TLoC) or syncope; 19/55 (34%) with symptoms or a diagnosis of postural tachycardia syndrome (PoTS). Ages ranged from 2–17 years (median 13; IQR 8–15), and 34/55 (62%) were female. 37/55 (67%) were referred by hospital or community-based paediatricians; 27/55 (49%) came from outside the paediatric neurology catchment area. Final diagnoses included 10/55 (18%) with Reflex Asystolic Syncope (RAS), 17/55 (31%) with Vasovagal Syncope (VVS), 9/55 (16%) with orthostatic intolerance not otherwise specified, and 13/55 (24%) with PoTS. Treatments included slow sodium, or slow sodium with fludrocortisone e.g. for those with VVS, and PoTS, and glycopyrronium for some with RAS. Outcomes for the 20 with TLoC and follow-up, demonstrated significant improvement in CGI in 13/20 (65%) by 1 year. Outcomes for the 15 with orthostatic intolerance, including PoTS, with follow-up, demonstrated significant improvement in in CGI in 11/15 (73%) by 1 year.
Conclusions: Half the patients were referred from outside our regional catchment area, suggesting a shortage of local expertise. Outcomes at one year were good in 2/3 -3/4, although we have no outcomes on patients discharged or lost to follow-up. We recommend therefore routine telephone follow-up at one year, of all patients seen. That the patients had failed to improve with general paediatric and local services suggests that the paediatric neurology syncope clinic was effective.

Poster 178

Epidemiological study of subdural haemorrhage in infancy in the Republic of Ireland

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Objectives: To describe the incidence, aetiology, and radiological workup of infants (>28 days) with subdural haemorrhage (SDH) in Ireland to inform management and prevention strategies.
Methods: New cases of SDH among infants (<12 months) were prospectively reported through the Irish Paediatric Surveillance Unit (IPSU), between November 2019-March 2021. Infants <28 days were excluded.
Results: There were 14 cases of infant SDH newly diagnosed by computerised tomography (CT) or magnetic resonance (MR) neuroimaging. This represents approximately 10 SDH/ annum i.e. 16/100,000 of the infant population in Ireland. The average age at presentation was 16.8 weeks. Ten (71.4%) infants underwent CT and 12 (85.7%) MR imaging of whom 4 (28.6%) had MR imaging alone. Eight infants (57.1%) had both CT and MR imaging. Six (42.8%) infants had cervical spine imaging of whom only 4 (28.6%) also had whole spine views. There were 11 (73.3%) skeletal surveys, 3 of which demonstrated fractures. There were only 5 (35.7%) repeat skeletal surveys and no new findings. Of 4 infants determined to have abusive head trauma (AHT), 3 had multiple SDH, 2 had associated subarachnoid haemorrhage (SAH), and one had a skull fracture. Four infants had accidental injuries including 3 falls and one impacted by a falling object. Two infants with accidental injury had multiple SDH, one had associated SAH and 3 had skull fractures. There were 5 organic causes of SDH, none with associated SAH or skull fractures. The single case for which an aetiology was undetermined had multiple SDH, with no other abnormality.
Conclusion: In Irish infants >28 days of age, the presentation and pattern of injury differs between accidental/organic causes of SDH and AHT. This has implications for management and practice guidelines. In contrast to previously published epidemiological studies, AHT appears not to be the predominant cause of SDH.

Poster 179

Etiologies of lumbar puncture refusal in pediatric patients in Taif children's hospital, Saudi Arabia. A cross-sectional study

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Background: Lumbar Puncture (LP) is a medical emergency operation in which a needle is inserted into the lower back's spinal canal for diagnostic and therapeutic purposes. Even though LP has a high diagnostic and therapeutic value, many parents refuse to have their children tested.

Objectives: To assess the misunderstanding regarding LP among parents in Taif city.
Methods: A cross sectional study was done on 687 of parents of children who required LP procedure from birth till the age of 18 in Taif Children's Hospital from January 2020 to February 2020. Data about participants demographics, ever been asked to take a sample of the cerebrospinal fluid (LP) of the child, circumstances related to this event were collected. For those who were not asked for, a question of "if it was needed to take a sample of the cerebrospinal fluid of one of your children, will you agree?", was added.
Results: 15.7% of parents were asked to take a sample of the cerebrospinal fluid of one of their children, of them, 61.2% agreed, with the average age of the child at the LP being 2.24 ± 3.28 years. A consultant discussed the LP technique to 37.8% of them, and 86.5% and 56.2% said the doctor clarified the nature and complications of the treatment to them. For parents not asked for LP before, 41.4% will not agree for it in the future. For parents who refused LP when indicated and hose refusing it in the future, the most common causes were the side effects as paralysis (60.6%), pain (11.3%) and no trust in HCWs and fear of medical errors (10.9%). For them, the most common sources of refusal were information from friends and relatives (41.2%).
Conclusion: There is a need for health education of parents about the importance and nature of LP to overcome barriers that lead to LP refusal.

Poster 180

Is functional illness in children always associated with anxiety or depression? Learning points from a specialist service

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Objective: Patients with functional illness have physical symptoms which cannot be adequately explained by organic pathology. Whilst there is a strong association between paediatric functional illness and comorbid anxiety and depressive symptoms, not all children with functional illness have clinically diagnosable anxiety and depression. Clinicians, children and families can often be skeptical of a diagnosis of functional illness in the absence of reported stress or anxiety and depression. This study aims to evaluate the prevalence of anxiety and depression in paediatric functional illness.
Methods: The study population includes patients enrolled at Function First, a multidisciplinary service at the Royal Alexandra Children's Hospital for children with functional symptoms, between December 2017 and September 2020 who had measures of anxiety and depression recorded. Anxiety and depression were measured using the Revised Children's Anxiety and Depression Scale (RCADS) questionnaire, completed by both parent and child at the beginning and end of treatment.
Results: RCADS questionnaires were completed by 37 children at baseline, 30.6% of these children had a Total Anxiety and Depression score (TAD) above the diagnostic threshold (RCADS >70). TAD score decreased post-treatment; from an average of 59.8 pre-treatment to 54.9 post-treatment.
Conclusions: The prevalence of anxiety and depression in this cohort was lower than expected, indicating that a diagnosis of functional illness is still appropriate in the absence of apparent anxiety and depression. The lower than expected anxiety and depression may be due to alexithymia, the inability to recognise one's own emotional states, which is common in children with functional illness. The multidisciplinary management resulted in reduced TAD scores supporting the efficacy of services like Function First to treat paediatric functional symptoms.

Poster 181

Defining the phenotype of male patients with c.320A>G variant in ALG13

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Background: Congenital disorders of glycosylation (CDG) are a group of neurometabolic diseases that result from genetic defects in the glycosylation of proteins and/or lipids. ALG13 mutations lead to a defect in the protein N-glycosylation process. Pathogenic variants in this gene have been implicated in the aetiology of epileptic encephalopathies and intellectual disability (ID), specifically, developmental and epileptic encephalopathy 36 (DEE36). The clinical course is very variable among individuals with CDG. The NM_001099922.3:c.320A>G:p.(Asn107Ser) variant is one of the most frequently described mutations in ALG13. The clinical course is very variable among individuals with CDG. To date, there have been 56 affected females and only 2 affected males reported with this variant.
Case Report: We report on a third male with the NM_001099922.3:c.320A>G:p.(Asn107Ser) variant in ALG13 whose phenotype is very similar to the two previously reported male individuals. He presented at 9 months of age with infantile spasms, which were difficult to control, and developmental delay. He progressed into a developmental and epileptic encephalopathy with severe ID, and continues to have drug-resistant epilepsy. Other features include feeding difficulties, skeletal abnormalities, recurrent infections and a movement disorder. Physical examination revealed he was symmetrically small with facial dysmorphism, clindodactyly of fingers and toes, and hypotonia. An extensive metabolic workup, including transferrin isoforms and APO3 isoforms were all normal. Whole-exome sequencing revealed a de novo hemizygous mutation in ALG13 gene, NM_001099922.3: c.320A>G:p.(Asn107Ser).
Discussion: Despite the small sample size, we suggest that there may be a detectable phenotype in males with the c.320A>G variant in ALG13 when compared to males with other variants in ALG13. They characteristically have de novo mutations, developmental and epileptic encephalopathy with drug refractory epilepsy, ID, dysmorphism, recurrent infections and a movement disorder – a phenotype not consistently seen in other variants in ALG13.

Poster 182

Use of the blink reflex in a paediatric clinical neurophysiology department – a service evaluation

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Background/Objective: The blink reflex is the neurophysiological counterpart of the corneal reflex and provides an objective tool for testing the integrity of cranial nerves (CN) V and VII. Electrical stimulation is applied to the supraorbital branch of CNV, and responses are recorded in orbicularis oculi. The main responses comprise the ipsilateral R1, reflecting a disynaptic connection between CNV and CNVII nuclei, while the bilateral R2 component reflects a polysynaptic pathway between CNV and the ipsilateral and contralateral CNVII nuclei, passing through the trigeminal spinal nucleus and medulla. We performed a retrospective review of our practice to evaluate use of this test in a paediatric setting.
Methods: We searched our clinical database from January 2019-January 2020 for all patients in whom a blink reflex had been performed. We reviewed the age, referral question, results and interpretation of each case.
Results: 64 patients were identified. Age distribution was as follows: 15 age <=2years (23.5%), 25 age 2–4yrs (39%), 17 age 5–10yrs (26.5%), 7 age >10yrs (11%). The referral question was to investigate for bulbar palsy in 49 (76.5%), facial weakness in 9 (14%), possible Guillain-Barre/Miller Fisher in 3 (5%) and other reasons 3 (5%). R1 components were normal in 50 (78%) patients, abnormal in 4 (6.3%), borderline in 3(4.7%), unsatisfactory in 7 (11%). R2 components were normal in 23 (35.9%), abnormal in 6 (9.4%), not seen in 29 (45.3%) borderline in 1 (1.6%), unsatisfactory in 5 (7.8%). Blink reflex abnormalities supported diagnoses such as bulbar palsy, moebius syndrome, a pontine lesion, or, when combined with EMG changes, widespread denervation.
Conclusion: Satisfactory blink reflex recordings can be obtained in most children and provide clinically useful information regarding cranial nerve function: An abnormality of R1, which is usually very robust even in young children, is clinically very significant. Whilst R2 components are difficult to elicit in younger children, when present but delayed/asymmetrical, this is also significant.

Poster 183

Lumbar puncture manometry: A snapshot of practice in the East of England

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Objective: Measurement of intracranial pressure through lumbar puncture (LP) manometry can provide critically important information for patient management. We informally observed that regionally manometry was rarely performed in LP, with consequent impact upon procedural confidence. We designed a survey to investigate current practices in LP manometry in the East of England and how knowledge of and confidence in this skill can be developed.
Methods: Electronic survey distributed to paediatric consultants and trainees in the East of England between February and June 2021.
Results: 18 consultants and 40 trainees participated. 86% (50/58) respondents reported performing manometry in less than 10% of LPs, with 45% (18/40) trainees never having used a manometer. 48% (19/40) trainees noted they had never had any instruction in using a manometer. Mean confidence with the procedure was 2.8 (5 point Likert scale). All consultants described capability to perform manometry in their hospital (usually if planned in advance), but 40% (16/40) of trainees were not certain. 79% (46/58) of participants identified "relative infrequency of the procedure with lack of confidence in performing" as amongst the greatest challenges. 75% (30/40) trainees also felt "insufficient training or knowledge" presented a challenge in conducting the procedure. "The availability of a guideline" covering manometer usage and interpretation of findings was the most suggested intervention (79%, 46/58) to improve skills.
Conclusions: The results support our observation that LP manometry is not performed routinely – potentially due to nearly half of trainees reporting having had no training in it. There appears to be a consequent impact upon confidence with the procedure. Inability to measure and address raised intracranial pressure using LP manometry could adversely affect patient management. We therefore recommend that competency in manometry is considered mandatory for trainees. Clinicians should be empowered to develop their skills and experience through provision of educational resources.

Poster 184

My Neuro Survey: preliminary paediatric findings of the 2021/22 national neurological patient experience survey

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My Neuro Survey is the fourth iteration of The Neurological Alliances biennial National Neurological Patient Experience Survey. The survey presents a comprehensive picture of the experiences of people living with a neurological condition. For the first time this includes children and young people living with a neurological condition thanks to the development of a questionnaire specifically for use in paediatrics. The survey will run online and in select neurology and paediatric neurology clinics between October 2021 and January 2022. The paediatrics research covers a wide range of topics including the impact of COVID-19, diagnosis, hospital care, support for mental wellbeing, access to additional support and education. The 2018/19 survey constituted the largest ever patient experience survey of people with neurological conditions in England with 10,339 responses. With the addition of paediatrics and rollout in all four nations of the United Kingdom, we are hopeful of even more responses and as such an even more robust dataset in 2021/22. Our ambition is to present preliminary survey response data from the paediatric survey alongside initial key themes ahead of full publication scheduled for the end of March 2022. The 2018/19 survey showed that significant unwarranted variation in care, with too many adults with neurological conditions facing long waiting times, poor access to specialists and a lack of personalised care. The survey also found evidence of failings in the social care and welfare systems, and discrimination in the workplace. Relevant data was used in major patient organisation campaigns, to support the business case for new resources and to provide the patient perspective in calling for improved services.

Poster 185

How useful to paediatric neurology Grid training are out of hours shifts?

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Introduction: Most paediatric neurology training in the UK currently involves successful completion of a Grid training programme run through tertiary paediatric neurology centres, with training supervised by the BPNA and RCPCH College Specialty Advisory Committee. Training often includes participating in an out-of-hours on-call rota, with the rota and roles undertaken varying significantly amongst training centres. This study reviewed the perceived usefulness of out-of-hours shifts towards their paediatric neurology training amongst Grid trainees in the UK.

Methods: All paediatric neurology Grid trainees working in the UK in February 2021 were invited to participate. Data was collected over five months (February to June 2021) on the shift worked (evening, night, weekend, bank holiday), clinical areas covered, number of cases seen, number of cases deemed relevant to paediatric neurology training and acute/emergency neurology, and if relevant to training, to which domain of the Grid curriculum the case related.

Results: 6/19 (32%) Grid trainees in clinical training posts at the time of the study participated. Data was collected on a total of 39 shifts (24 nights, 9 evenings and 6 weekends). Significant variation was seen in the clinical areas covered; 33/39 (85%) shifts covered either general paediatrics or the emergency department. No shift solely covered paediatric neurology/neurosurgery. In total, 294 cases were seen, with 40/294 (13.6%) being deemed relevant to paediatric neurology training and 17/294 (5.8%) being deemed relevant to acute/emergency neurology training.

Conclusions: Most paediatric neurology Grid trainees undertake out-of-hours work in some capacity during their training. In no centre was this solely covering neurology/neurosurgery; most trainees cover general paediatric wards and/or admissions, or a combination of subspecialty wards. Out-of-hours training is often justified as providing exposure to acute neurology presentations; however, only 5.8% of cases were felt to provide this. Most cases seen related to general paediatrics rather than neurology subspecialty training.

Poster 186

Changing from liquid medicines to tablets in children over 5 years

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Objective: This study aims to highlight the benefits to families and service providers in changing from liquid medicines to tablets in children over 5 years.

Methods: Using data provided by Bolton Clinical Commissioning Group (CCG), for 5–14-year-olds, we were able to analyse the average cost per item and volume of prescribing for 20 different tablets and liquids over one year. We analysed examples of cost savings for the same dose of drug per week or year based on the cost of a typical 28-day supply. We designed a suggested practice for positive change along with signposting to educational materials and specific considerations for children with neurodisability.

Results: There are economic benefits to prescribing tablets rather than liquids for children over 5 years whenever possible e.g., for flucloxacillin liquid the cost per item was £27.82 with 2140 items prescribed. In comparison, the tablet form was £1.81 with 1123 items prescribed. If half liquids were prescribed as tablets, this would save £27,820. Similarly, nitrazepam gave a saving of £19,482, oxybutynin £14,904, melatonin £10,996, diazepam £8,192 and baclofen £1,595. The results showed a total annual saving of £117,314 for all 20 drugs if half liquids were prescribed as tablets.

Conclusions: There are positive incentives for families, safety and economic benefits to prescribing tablets rather than liquids for these children. Liquids have shorter expiry dates, often require refrigeration and may be difficult to obtain locally. Liquids can be unpalatable, cause tooth decay and can vary in concentration. Dosing errors may occur in families with low health literacy or language problems. Out of the 20 medications included in our study, 15 could be crushed or dispersed to help patients with neurodisability. Increased awareness of these benefits amongst prescribers and supporting families should lead to a positive change.

Acknowledgements: Thanking Bolton CCG for data.

Poster 187

Unusual cause of episodic encephalopathy

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A 15 year old boy presented with acute prolonged episode of encephalopathy, and slurred speech associated with headache and vomiting. This was not preceded by head injury, fever, or drug misuse. Past medical history revealed recurrent episodes of confusion associated with visual disturbance and paresthesia that last for few hours and resolved spontaneously. These sometimes were associated with headaches, occurring twice yearly for the last three years. Family history was remarkable for migraine in mother. Examination was consistent with mild encephalopathy in the form of confusion, slurred speech and mild right-side hemiparesis. Initial differentials considered with presentation of episodic encephalopathy with mild hemiparesis were focal seizures with Todd's paresis, channelopathies including hemiplegic migraine, recurrent demyelination, acute decompensation in a metabolic disorder and transient ischaemic events. MRI head was normal, EEG captured focal abnormal slow activity over the left anterior quadrant. Metabolic investigation, auto immune workup for autoimmune encephalitis and anti TPO were negative. Over three weeks admission, right side hemiparesis resolved within few days, however confusion took three weeks to normalize and speech difficulties improved in 8 weeks time. Given his presentation and family history we suspected familial hemiplegic migraine and subsequently genetic test revealed heterozygous mutation for likely pathogenic ATP1A2 missense variant, ATP1A2 confirming the diagnosis of hemiplegic migraine type 2. He remained well on calcium channel blocker flunarizine and adherence to healthy life style modification for migraine prevention. No further hemiplegic migraine episodes recurred since.

Discussion: Hemiplegic migraine is a rare subtype of migraine with aura, characterized by the presence of motor weakness as an aura manifestation. Typically, migraine aura has visual symptoms, but occasionally impairment in sensation, speech or motor weakness

may be seen. Familial hemiplegic migraine (FHM) is inherited as autosomal-dominant, and is classified into 4 subtypes based on the genetic mutation associated with them (CACNA1A, ATP1A2 and SCN1A). It is important for clinicians to be aware of FHM as a cause of episodic confusion and encephalopathy which can sometimes occur without significant hemiparesis.

Poster 188

Seizure recognition in paediatric critical care: Are we setting up our front-line trainee clinicians for failure?

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Background and Aim: Seizures occur frequently in critically ill children. Gold standard seizure detection using multi-channels electroencephalograms (EEG) requires expert interpretation that is unsustainable at the critical care bedside. We are then reliant on our front-line clinicians to recognise seizures at the critical care bedside. This pilot study aims to determine trainee clinicians' confidence in seizures recognition in critical care and their experience in EEG interpretation and training.
Method: A prospective pilot survey study was conducted over a one-month period. Medical trainees and advanced nurse practitioners (ANP) were invited to complete a pre-designed online questionnaire to determine their confidence in diagnosing seizures, when a seizure terminates with treatment, and their experience with prior EEG interpretations.
Results: 20 acute paediatric clinicians (18 trainees and 2 ANP) participated in the survey (response rate of 100%). Only half of the participants reported confidence in clinical seizure recognitions. 85% reported no confidence in recognising seizure activity on EEG in critically unwell children. 80% reported no previous formal training in EEG interpretation, despite this 55% had to interpret EEG data previously within their clinical role, with 40% doing so during out of hours. 95% felt a quantitative seizure detection tool would increase their confidence in seizure recognition.
Conclusion: In this pilot study, acute paediatric clinicians are not confident in recognising clinical and electrical seizures with the majority reporting they would benefit from having formal training and a quantitative seizure detection tool. This warrants further investigations to improve seizure detection and patient safety in critical care unit.

Poster 189

Non-expert seizure detection on multi-channel electroencephalograms in the paediatric critical care unit: Room for improvement

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Background and Aims: Prompt recognition and treatment of seizures improve the neurological outcome of critically ill children. Seizure recognition accuracy on multi-channel electroencephalograms (EEG) by non-expert clinicians is unknown. This study aims to assess the electrical seizure detection accuracy of non-expert clinicians
Methods: A prospective observational simulation study was performed. Medical trainees and advanced nurse practitioners (ANP) were invited to review screenshots of 20 fully anonymised multi-channels EEG traces in a simulated intensive care (ICU) setting. These were obtained from an open-source EEG database or from a consultant paediatric neurologist specializing in epilepsy (AM). Seizures were pre-identified on the study EEG by AM (i.e. expert gold standard). The participants were asked to state whether they identified a seizure or not as they reviewed the EEG traces in real-time with the same researcher (VR) present recording their findings. Their results were compared with the expert gold standard to determine the accuracy of seizure detections.
Results: 18 medical trainees and 2 ANP participated in this study. Of the medical trainees, 6, 7, and 5 were respectively at junior, middle, and senior training levels. Participants accurately diagnose 59.25% electrical seizures in the 20 study EEG traces. Sensitivity was 44.78% (95% CI 38.24% - 51.46%) and specificity 78.24% (95% CI 71.27%- 84.19%).
Conclusion: We found a low detection accuracy of electrical seizures amongst our participants. Formal EEG interpretation training may enhance seizure detection accuracy of our front-line clinicians and warrants further investigation.

Poster 190

Impact of Distance Learning Groups for completion of BPNA Modules

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Objective: To evaluate the impact of learning groups on completion of BPNA distance learning courses.
Methods: A survey was emailed to participants of learning groups followed by two reminders. Groups had collaborated via Zoom meetings to complete BPNA modules on 'Epilepsy' (2), 'Neuromuscular Disorders' and 'Cerebrovascular Disease, Trauma and Coma'.
Results: The anonymous survey was emailed to 53 participants with a 57% response rate. 5 responded for multiple modules. Participants included 5 consultants, 6 clinical fellows, the remainder trainees of varying levels. 36% were SPIN, 25% GRID training and others participating for professional development. Participants came from 10 deaneries across the United Kingdom and Ireland. 54% reported discovering the groups through word of mouth. 96% rated the set-up communication as good or excellent. All agreed the groups increased their understanding. 89% responded the groups improved their confidence in managing the conditions. Over 80% responded the sessions were relevant and pitched correctly. 89% responded the sessions prompted further reading. 93% responded consultant neurologists facilitated most of the sessions and all responded that this improved quality. Participants struggled to balance workload with 21% feeling unable to complete the written content prior to the sessions. A break every 4–5 weeks was suggested to allow catch-up, 64% in favour. 64% want the sessions to be recorded in future. Of these,

48% want sessions saved to the BPNA website, similarly 45% (15% each) wanted sessions saved to Google Drive, MS Teams or shared by the presenter. Respondents requested that recorded sessions be restricted to participants, to encourage informal discussion. Participant feedback on teaching is needed; 29% did not receive this.
Summary: 96% of participants would recommend learning groups and 100% felt the BPNA should organise these, indicating their success in creating an interactive learning environment for the completion of online modules.

Poster 191
Functional Neurological Disorder: A feasibility pilot for a hybrid inpatient and virtual outpatient rehabilitation placement

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Objectives: To assess the feasibility of a multidisciplinary rehabilitation package for functional neurological disorder (FND)/functional motor disorder (FMD) at The Children's Trust (TCT)
Method: A 20 week package was developed by reviewing the literature and existing models, consisting of 1–2 weeks inpatient followed by virtual outpatient sessions. Input was provided from: (1) Clinical psychologist; (2) Physiotherapist; (3) Occupational therapist; (4) Consultant in Paediatric Neurodisability; (5) Educational psychologist. This was delivered to an adolescent boy (SK) with FND. He presented with gait disturbance resulting in falls, non-epileptic seizures, tics and fatigue. SK's goals were to: (1) Complete his morning routine; (2) Spend time with friends without subsequently 'busting'; (3) Spend a whole day with his family in an activity; (4) Manage his racing thoughts. The approach to management was cognitive behavioural therapy (CBT) based. SK developed and trialled his own self-management strategies. Fatigue was SK's predominant symptom and the initial focus of management. SK's family and school also had input to understand management of FND/FMD.
Results: SK achieved his goals, with improvement in performance and satisfaction on the Canadian Occupational Performance Measure. The frequency and severity of his FND symptoms substantially reduced. SK reported he had a toolkit to manage FND in all areas of his life. It was noted that as SK learnt to manage his fatigue other symptoms substantially improved, and only recurred with fatigue. Traits suggestive of autism spectrum disorder (ASD) were identified and SK has been referred for assessment.
Conclusions: The feasibility of delivering a predominantly virtual outpatient multidisciplinary rehabilitation package for FND has been demonstrated. A multidisciplinary CBT based approach to FND can improve symptoms and participation. Management of significant non-neurological symptoms can improve neurological symptoms. This is important for services that lack experience of FND but have managed chronic fatigue or chronic pain. Consistent with the literature, ASD is an important diagnosis to consider.

Poster 192
Fanconi Syndrome – a rare life threatening complication of sodium valproate

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Objective: Sodium valproate is a commonly used antiepileptic medicine in paediatrics. Although generally well tolerated, Valproic acid (VPA) can occasionally cause side effects like liver dysfunction, hair loss and pancreatitis. There are a few case reports of Fanconi syndrome due to Sodium Valproate. We describe a life threatening case of Sodium Valproate induced Fanconi syndrome in a child with epilepsy and complex neurodisability.
Methods: Data was collected from the hospital notes of a 4 year old girl with a background of ERMARD gene mutation, severe global developmental delay and epilepsy. She was on ketogenic diet, VPA and gastrostomy feeds. She presented with signs of respiratory infection, drowsiness and increased urine output.
Results: Her blood tests showed a pH of 6.98 with base excess of -24.7, serum sodium 177mmol/L, Potassium 3.3mmol/L, Chloride >140mmol/L, Bicarbonate 7.3mmol/L, Creatinine 94 mmol/L, and serum Osmolality of 363mmol/kg. Urine analysis showed osmolality of 267mmol/kg, phosphate 3mmol/L, Sodium 29mmol/L, Potassium 7.7mmol/L, Glucose ++++, Protein +++. Blood results and urine analysis were suggestive of dehydration and severe metabolic acidosis due to renal loss of water, protein, glucose and bicarbonate. All these pointed towards the diagnosis of Fanconi syndrome. Her management included discontinuation of Sodium valproate, replacement of bicarbonate, hydration and inotropic support. All metabolic parameters normalised over a month after presentation.
Conclusions: Fanconi syndrome can be a rare life threatening but reversible complication of Sodium Valproate. It affects children with developmental delay, reduced mobility and tube feeding dependence. This may be due to their inability to communicate thirst. In children with complex disabilities and on Sodium Valproate, Fanconi Syndrome should be considered as a cause for unexplained renal tubular acidosis as prompt recognition and treatment will have a favourable outcome.