Abstract’s For JNNP

Poster session THUR, 001

An unusual (ne)urological presentation

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We present the case of a 78-year-old female with a background of diabetes, who presented with acute-onset hemichorea whilst on the surgical ward under the care of the Urology team. She had an extensive past medical history including type two diabetes; additionally, she reported she had experienced similar transient symptoms during an admission ten months previously. CT and MRI brain demonstrated no acute ischaemic changes. A thorough drug history revealed no causative agent, and her blood tests were unremarkable. Her capillary blood glucose charts showed a severe hypoglycaemic episode two days prior to the onset of symptoms with similar hypoglycaemic episodes noted during her last admission. A diagnosis of hypoglycaemia-induced hemichorea was made and the patient was started on tetrabenazine. Our case of an elderly diabetic patient with new-onset hemichorea secondary to hypoglycaemia highlights the importance of identifying and optimising glycaemic control in this vulnerable cohort.

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Poster session THUR, 002

An unusual presentation: two aetiologies for the price of one!

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70-year-old female receptionist presented with acute onset lower back pain whilst sitting down. She tried to weight bear but felt her left leg "gave way". There were no sensory complaints and no sphincter disturbance. Positive examination findings in her left lower limb include reduced tone, power 2/5 throughout, and left extensor plantar. In addition, she had absent knee and ankle reflexes bilaterally and loss of pinprick and temperature sensation on the right side up to L1 dermatome, with preservation of vibration and proprioception. She had a normal sensory examination of her left lower limb and rectal examination was unremarkable. Clinically, she has an atypical form of Brown-Séquard syndrome with weakness in the left lower limb and sensory loss in the right lower limb with a sensory level. MRI lumbar/sacral spine showed L3 slipped anteriorly with L3/4 disc bulge resulting in cauda equina syndrome. She was re-scanned five days later including thoracic spine and found to have an acute left hemi-cord infarct at T8/9. This case demonstrates the importance of scanning the relevant sections of the cord and to keep a broad differential in mind, as there can be two aetiologies at work which might misguide the clinician at first glance.
**Poster session THUR, 004**

Foramen magnum decompression for tonsillar herniation secondary to meningoencephalitis

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Tonsillar herniation and coning is a rare complication of meningoencephalitis and is associated with poor neurological outcome. Our patient presented unresponsive with radiological evidence of tonsillar herniation secondary to meningoencephalitis. She underwent an emergency foramen magnum decompression and C1 laminectomy with full recovery.

16 years old female presented to her local ED with headache, vomiting, hallucinations, photophobia and neck stiffness. Her CT head was normal. She was commenced on acyclovir and ceftriaxone on the same day and clinically improved. LP performed 24 hours later showed WBC of 226 (200 lymphocytes, 6 polymorphs), protein 1.2g/l, negative MC&S, negative viral PCR, negative TB PCR. CSF glucose was not sent. In light of a predominantly lymphocytic CSF and presumed viral meningitis antibiotics were stopped. Three days later acutely deteriorated. MRI head showed evidence of tonsillar herniation. She was restarted on antibiotics and was transferred to tertiary centre. She underwent emergency insertion of an EVD, foramen magnum decompression and C1 arch laminectomy. She made a full recovery with no residual neurological deficit.

The mainstay treatment of meningoencephalitis is intravenous antibiotics. However, in cases complicated by tonsillar herniation with reactive pupils, foramen magnum decompression should be considered.

**Poster session THUR, 005**

Two atypical presentations of PRES?

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Posterior reversible encephalopathy syndrome (PRES) is characterised by acute neurological symptoms with vasogenic oedema typically in parieto-occipital lobes. PRES involving atypical locations is becoming increasingly recognised. Here we report two atypical cases.

An 83-year-old male with ureteric carcinoma presented with confusion, headache and high blood pressure (170/80). MRI revealed symmetrical temporal lobe T2-hyperintensities with no mass-effect or restricted diffusion. He was treated for presumed viral encephalitis. CSF was negative. Seizure was treated with Levetiracetam. Three weeks later MRI showed worsening of temporal lobe T2-hyperintensities with mild mass-effect and one small area of restricted diffusion. Despite no treatment for hypertension, six weeks later MRI showed significant improvement. Gradient echo demonstrated multiple microhaemorrhages consistent with hypertension.
A 69-year-old female presented with discitis, sepsis, fluctuating consciousness and high blood pressure (180/90). Patient reported hearing a song recurrently which could represent ‘musical hallucination’ associated with seizure. CSF was normal. She was treated with Levetiracetam. MRI showed symmetrical fronto-temporal lobe T2-hyperintensities with no mass-effect and small area of restricted diffusion. Although hypertension was not treated, one week later MRI improved significantly.

In summary, MRI appearances improved in both with minimal intervention. The underlying aetiology may remain elusive, but could these be atypical presentations of PRES?

Poster session THUR, 006
A case of GABA-B antibody mediated encephalopathy

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A previously well 17-year old female presented with a self-limiting episode of derealisation and depersonalisation lasting 24 hours. Initial MRI demonstrated new left peri-trigonal white matter hyperintensity. Initial bloods were normal and serum was negative for white cell enzymes, VLCFA and broad autoimmune screen but positive for GABA-b antibodies (Ab).

Six months later, an acute cognitive decline, intermittent upper limb tremor and emotional lability led to readmission. On examination she had an ACE-R of 88/100 and mildly slowed saccades. Repeat MRI was stable and EEG was diffusely slow, particularly the right temporal lobe. She had a mild CSF lymphocytosis (8 cells). An underlying malignancy was excluded with CT chest, abdomen, pelvis and PET CT. She was treated with PLEX and pulsed intravenous methylprednisolone, which led to an improvement of her symptoms and cognitive status. She was discharged on oral steroid taper. One month later she had a milder relapse and was retreated with PLEX and started on mycophenolate. She has now been in remission for 18 months.

Conclusions: Our case highlights that neurologists should consider GABA-b Ab mediated encephalitis as a differential in patients presenting with derealisation and depersonalisation, in addition to previously described presentations of seizures and ataxia.

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Poster session THUR, 007
A garden variety neuropathy

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A 47 year old with subacute onset of walking difficulties, asymmetric lower limb and facial weakness and areflexia was admitted as a suspected case of Guillain-Barre syndrome. Clinical examination revealed left lower motor neuron facial weakness, right upper limb and lower limb weakness and a suspended area of pain and allodynia at T7. Structural imaging of the brain and spine was normal. CSF protein was elevated with pleocytosis.
Nerve conduction studies was suggestive of proximal demyelinating polyradiculoneuropathy. The clinical suspicion of neuroborreliosis was confirmed in CSF with Borrelia VlsE antigen positivity and serum Borrelia Burgdorferi IgG EIA positivity. The patient had no recollection of tick exposure but did recall a presumed horsefly bite on the forearm two weeks earlier of uncertain significance. This is a case of Bannwarth syndrome - meningoradiculoneuritis due to neuroborreliosis endemic in Northern Europe. Our patient was treated with Ceftriaxone with rapid improvement of symptoms. This case highlights the importance of careful history taking including ascertainment of travel to Borrelia endemic areas and recognition of this eminently treatable meningoradiculoneuropathy.

Poster session WED, 011
Subacute combined degeneration of the cord: Laugh until You Are Weak

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A 33 year old lady presented to her GP with a 2 week history of numbness affecting her thighs. Routine blood tests revealed normal haemoglobin and folate levels with a borderline B12 concentration of 103 ng/L. Over the subsequent 2 weeks the numbness spread to involve her feet and her hands. Despite commencing cobalamin injections her symptoms continued to progress. She was admitted to hospital 4 weeks after the onset of symptoms with disabling sensory ataxia.

All reflexes were either absent or elicited only with reinforcement. Plantars were downgoing. There was impairment of all sensory modalities in a glove-and-stocking distribution, with proprioception accurate at the ankle on the right and the knee on the left. Her gait was broad-based. The remainder of the neurological examination was unremarkable.

A full peripheral neuropathy screen revealed no abnormality. An MRI spine showed longitudinally extensive myelitis mainly affecting the dorsal cord extending from C4 to T3. MRI brain and lumbar puncture were pristine.

Guided by the MRI findings direct questioning elicited a long history of frequent recreational nitrous oxide use. We review the accumulating literature regarding nitrous oxide-induced subacute combined degeneration of the cord and explore the pathophysiological mechanisms underlying it.

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Poster session WED, 012
Reversible optic neuritis secondary to metronidazole

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Metronidazole is a nitroimidazole antibiotic used to treated anaerobic bacteria and protozoal infections. Neurological side-effects are documented mainly relating to
peripheral neuropathy. There are only isolated case reports of optic neuropathy secondary to Metronidazole. We describe a 36 year old man who presented with reduced central visual loss on a background of a two year history of Metronidazole use for a perianal fistula. Electrophysiology confirmed bilateral optic neuropathy. On cessation of Metronidazole visual acuity and electrophysiological studies returned to normal. This is the reported longest duration of metronidazole at maximal dosing causing an optic neuropathy with complete resolution on cessation.

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**Poster session WED, 014**
OCT minimises unnecessary investigation for suspected papilloedema

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Background: Optical coherence tomography (OCT) is a rapid and painless way to provide a record of the optic disc structure. Though not specific, it can identify swollen optic discs. We determined the impact of OCT prior to referral on the pathway for managing suspected papilloedema.

Methods: Audit of adults referred from the Western Eye Hospital to St Mary’s Hospital with suspected papilloedema was performed between 1/1/17 and 16/5/17. A follow-up re-audit was performed from 1/6/17 to 31/8/17 following implementation of OCT prior to referral.

Results: The initial audit identified 50 patients over 136 days and the re-audit 26 patients over 92 days. In the initial audit 6/50 had OCT and 17/50 (34%) were admitted. 6/50 patients were subsequently found not to have papilloedema on fundoscopy, none of whom had OCT. 4/6 underwent unnecessary neuroimaging and lumbar puncture. 3 were admitted, equating to 18% of all admissions, for an average of 2.3 days. In the re-audit all had OCT, 6/26 (23%) were admitted and none were subsequently found not to have papilloedema.

Conclusion: Use of OCT prior to referral for suspected papilloedema helps to reduce unnecessary investigations.

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**Poster session WED, 016**
A service evaluation of the acute neurology clinic

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Rationale: Neurological symptoms are a common presentation in primary care and emergency medicine. The acute clinic provides a rapid access service, aimed at reducing unnecessary admissions, outpatient waiting times, inappropriate investigations and achieving a prompt diagnosis. Data on service utilisation will inform future service design and delivery.
Aim: To evaluate the acute neurology clinic service and training experience in the
University Hospital of Wales.

Method: Data was collected prospectively on acute referrals over 6-months.

Results: 52 patients were seen; 51% were referred from primary care. The median slots
filled per clinic was 3 (range 1-6). Median time from referral to review was 3 days (range
1-7). The most common presenting symptom was headache (38%), followed by limb
weakness (25%). The commonest clinical syndrome was a myelopathy (15%) and 62%
had abnormal neurological signs. 75% of patients were investigated, 10% admitted and
7% discharged. In retrospect, 56% of patients warranted urgent referral.

Conclusion: The acute neurology clinic provides a useful service to primary care. This data
suggests it is presently under-utilised and that similar clinics and novel strategies could
be enlisted to help reduce admissions and waiting times, and help manage patients with
neurological symptoms in primary care.

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Poster session WED, 017
Call on me: expanding the consultant advice line for GPs
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Background: The Consultant Advice Line (CAL) is a service developed to provide telephone
advice for GPs within our catchment. The hours of this service were extended in early 2017
to increase its capacity for GPs seeking guidance on neurological issues as part our Neuro
Network Vanguard project.

Methodology: Data was routinely collected from calls received between 1st March and 30th
June 2017, and a sample of GPs completed an online survey after the call.

Results: Volume of calls has more than doubled since expansion, with calls spread evenly
through the week and from all CCG’s in our region. Feedback from GP’s was
overwhelmingly positive with an average ‘call usefulness’ score of 9.2/10, and 100%
saying they would use the service again. 40% reported the advice had avoided an
outpatient referral.

Discussion: The provision of equitable neurology services is challenging in the current
climate. New models of care such as this help to break down barriers between primary
and specialist care, reducing undesirable variation in access to acute neurology input and
reducing unnecessary referrals to secondary and tertiary care.

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Poster session THUR, 018
Advice and guidance: not so quick and easy
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Background: Waiting times for outpatient consultations are consistently under pressure, and delivery of the mandatory 18-week target from referral to completed review remains challenging. An Advice and Guidance scheme offers an opportunity to access neurological advice while reducing face-to-face consultation needs. We designed this project to develop the requirements, methods, audit and costing of sustainable neurological advice.

Methods: A DGH Neurology service worked with a local CCG comprising 18 GP practices. All 176 referrals and advice requests received during a 6-month pilot were considered for A&G instead of a clinic appointment.

Results: Advice was offered in 37% of cases overall (48 patients), but a net increase of 12% in face-to-face consultations was observed, as 28 (16%) of advice requests required clinic review. Headache and alteration of consciousness were common, and cases with an established diagnosis the most tractable for the ‘Advice Only’ option. GP referral quality was judged good, neurology satisfaction was reasonable, and a cost of at least £68 per episode was indicated.

Discussion: This pilot showed an increase in the number of face-to-face clinic reviews required. We suggest that other reported schemes may have not included advice requests that resulted in referrals in their metrics.

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Poster session THUR, 021
Transforming acute neurology: a 4 year study

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We present a novel approach to acute neurological care. The key is an acute neurology triage nurse, based in the medical admission unit as well as an epilepsy specialist nurse seeing every patient referred with fits on the day of admission, a designated acute neurology consultant and acute neurophysiology and neuroradiology links. We have designated this group, a hyperacute neurology team (HANT).

This study compares all admissions in 2014, the year before the team was established with 2015-2017. The total number of referrals has increased from 720 in 2014 to 1248 in 2017. The percent of patients seen on the day of referral has risen from 59% in 2014 to 92% in 2017.

Average length of stay for patients with a primary diagnosis of epilepsy has gone down from 4.1 days in 2014 to 3.4 in 2017. Multiple admissions for epilepsy has reduced from 28 in 2014 to 21 in 2017. Patients suitable for early discharge are seen in consultant or nurse «outpatient hot clinics» or nurse telephone clinics.

The cost of establishing this service has been relatively small (£106,000) and the service benefits enormous. We feel this model is worthy of wider debate.

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Poster session WED, 024
Acute model in Gloucestershire
We operate a consultant led “post-acute” model for Acute Neurology service delivery, with Advice and Guidance (an email service for GPs); attendance at twice daily “huddle” meetings on MAU; and inpatient e-referrals. We have two sites, 683 inpatient beds in Gloucester Royal, and 379 in Cheltenham General. 10-15 of these inpatient beds (in Gloucester) are flexibly allocated under neurology. We received 153 inpatient e-referrals over a 1 month audit (October 2017). 78% of these received an inpatient review (the remaining 22% were managed by email); 97% within 24 hours, 7 days per week; 100% by consultants. This averages 5 referrals per day (range 0-9). Patients can be transferred under neurology when beds are available (49 admissions/month). The reasons for referral included focal neurological deficits (27%), headache (21%), epilepsy (14%), movement disorders (10%), unexplained loss of consciousness or possible seizure (9%), altered consciousness (8%), neurological infections (3%), and scan abnormalities (3%). This rapid input is in line with the ABN’s Quality Standard for Unscheduled Care. The referral element of this service requires approximately 1.5-2 PAs on each weekday, and 1 PA on each weekend day. We are also about to start an acute neurology clinic (approx. 20 slots per week).

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Poster session WED, 026
‘Creating a Neurological Exam Template for Acute Medical Admissions’

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Introduction: There is sub optimal documentation of neurological exam findings in patient’s hospital records. Documented Neurological findings are often incomplete, omitted or scattered in various places in the clinical notes. This is important in the setting of acute neurological emergencies, where accurate documentation is vital in gauging potential deterioration/improvement in a patient’s condition.

Method: A chart review was performed on 80 patients referred to the Neurology consult service in St James’s Hospital between January-February 2018. All aspects of the Neurological exam findings documented in these charts were noted. A gold standard template for accurate recording of Neurological exam findings was then created and circulated to all Hospital NCHD’s. A repeat chart review was performed on 80 patients referred to Neurology Consults between March-May 2018 (following the circulation of this template) and results were compared.

Discussion: Record keeping varied according to different clinical parameters, being lowest for speech at just over 20% and highest for muscle power at over 70%. Globally there was a small but significant improvement (P Value <0.001) in the documentation rates of neurological exam parameters following circulation of the template. We plan to apply this template to all acute medical admissions in St James’s Hospital.

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Poster session WED, 027
Acute neurology in Glasgow

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Provision of acute liaison in-patient neurology reduces demand on neurology outpatient services, reduces unnecessary investigations and use of medical beds by patients waiting on in-patient neurology review and allows speedier access to necessary neurological services for those with a neurological illness.

The pressure on acute neurology beds at QEUH Glasgow is immense and there is considerable delay in patients waiting for admission to the ward. An audit of the acute on call service in mid 2015 showed a 100% increase in the number of phone calls received by the on call registrar when compared to a similar audit in 2008. The number of requests for ward visiting to review medical inpatients at the Queen Elizabeth University hospital increased by more than 100% over the previous year.

In June 2016 an Acute Neurology rota was introduced whereby a Consultant Neurologist supervised and delivered patient care for the acute neurology wards, referrals from medical wards & acute receiving, as well as twice a week acute neurology clinics. This has led to a significantly improved care for patients referred with neurological problems as perceived by trainees, consultants and referring medical physicians, as evident on a survey carried out in 2017.

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Poster session WED, 028
One person can make a difference: our experience in a busy London DGH

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Our Neurology unit is in a busy district general hospital; serving a deprived inner London community, providing a ward consultation service 5 days a week. The unit consists of 5 consultant Neurologists, a consultant Neuroradiologist and 2 specialist nurses. In 2016, a junior doctor was appointed. By analysing data from 10 months in 2015 and 2017; we assessed the impact on the delivery of Neurological care, before and after the appointment. The unit saw a 157% increase in number of patients seen, including a significant proportion now seen in ED and ambulatory care. This is equivalent to a minimum of 2 more patients each working day (n=872 vs. 1317). The percentage of patients seen on same day of referral (<12 hours) increased from 47% to 77%. The proportion of inpatients reviewed who were then followed up on the ward during their stay, increased from 13.9% to 35.5%, representing increased availability of continuing Neurology advice. The percentage of patients who waited more than 24 hours for Neurology input decreased from 14.9% to 5.83%. Our results support the appointment of a full time junior colleague to allow rapid, safe and ongoing Neurological input to patients and to support ED and admitting colleagues.

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Poster session WED, 031

Neuro hot clinics: direct access clinic for acute medical patients
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20% of acute medical patients present with neurological symptoms, yet are often managed by non-specialist acute physicians. This district general hospital (DGH) introduced a direct access neurology clinic, to reduce hospital admissions and improve access to neurological expertise for vulnerable patients. Patients would otherwise have been admitted to await ward consultation.

20 "Hot" clinic appointments each week were allocated by administration prior to discharge from the medical admissions unit. All appointments were within 48 hours. Common diagnoses were migraine, first seizure, and non-epileptic attack disorder and rarer presentations included 5 with transverse myelitis, 1 with cerebral vasculitis, and 1 with Hepatitis E related encephalomyelopathy.

243 patients were seen by a Consultant Neurologist in 9 months in this hot clinic, thus saving at least 243 bed days and £73,000. Only 4 of these patients were readmitted. The hot clinic required 4PAs of consultant time split across weekdays, at an estimated cost of £30,000 per annum.

This neurology acute clinic successfully provided front door neurological input, a vital service for GPs and patients, and made approximate annual saving of £70,000. Evidently, every DGH should consider implementing neurology "hot" clinics.

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Poster session WED, 033

Minimum prevalence of non-compliance recorded in an audit of antenatal care in a district general hospital joint obstetric epilepsy

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Epilepsy is among the leading indirect causes of death in pregnancy. A retrospective case review of 143 DGH patients with seizures (50 Idiopathic Generalised, 72 Focal 19 Dissociative) seen in a joint obstetric neurology antenatal clinic from 2015-2017 was undertaken. Systematic data collection was not possible owing to the retrospective nature of the audit, however, salient findings were: Of the cohort of 143, 25 were not taking any AED at booking (around 12 weeks). Of those on AEDs over 80% were on lamotrigine or Levetiracetam monotherapy. Most (87/143) had been seizure free pre-conception for at least 1 year. 11 of this group had breakthrough seizures. AED levels were checked on 57 patients (Lamotrigine – 48:Levetiracetam 9) and were undetectable in 10/57 (17.5%) at booking. Reasons for AED testing refusal & non-concordance (when present) were unknown. Of 11 patients losing seizure control during pregnancy 3 were non-concordant at booking.

Conclusion: Non concordance at booking was documented in 1 in 6. Loss of previous seizure control occurred in 11/87 (12.6%) of previously seizure free patients of whom 3/11 were nonconcordant. AED monitoring revealed significant non-concordance and may relate to subsequent loss of seizure control. A prospective study is planned.
Identification of biofluid markers of TDP-43 pathology

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Introduction: Frontotemporal dementia (FTD) is usually caused pathologically by either tau or TDP-43. Previous biofluid assays of TDP-43 have not so far proved to be sensitive or specific for identifying those cases with TDP-43 pathology.

Material and Methods: We set out to investigate the novel TDP-43 Simoa assay (Quanterix) assay in both plasma and CSF in a cohort of patients recruited from the University College London FTD observational studies with known or likely TDP-43 pathology (17), non-TDP pathology (13), and healthy controls (10).

Results: The mean [standard deviation] plasma TDP-43 concentration was higher in those with likely TDP-43 pathology (155.1 [223.4] pg/ml) than those with non-TDP pathology (112.39 [252.9] pg/ml), and healthy controls (50.0 [23.1] pg/ml), but the differences between groups was non-significant, with substantial overlap in concentrations between all three groups. The mean CSF TDP-43 concentration was 2.9 [0.3] pg/ml in those with likely TDP-43 pathology, 2.8 [0.4] pg/ml in those with non-TDP pathology, and 3.1 [0.5] pg/ml in healthy controls.

Discussion: The assay tested in this study does not accurately distinguish between those with likely TDP-43 pathology and either disease controls or healthy individuals. There remains an urgent need to develop a better biofluid assay for pathological TDP-43.

Poster session, Thurs 37

Ictal asystole: return to the history

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In these two adult cases of transient loss of consciousness (TLoC), careful history-taking revealed a stereotyped prodrome of déjà vu suggestive of focal seizures. One patient had an implantable cardiac monitor fitted, the other a 48-hour Holter monitor. Each patient subsequently had a typical event of déjà vu followed by TLoC with rapid recovery and for both, the monitor showed cardiac asystole corresponding with this event. A permanent pacemaker (PPM) was inserted in both patients. This abolished TLoC. In its absence, déjà vu became more frequent, intense, and prolonged for one patient, resolving with levetiracetam. The other patient had a post-PPM episode of déjà vu followed by a
generalised tonic-clonic seizure. It transpired that their lamotrigin had been withdrawn following PPM insertion. Seizure-freedom was achieved by restarting lamotrigin.

Ictal asystole, a rare complication of focal epilepsy, has a mean ventricular standstill duration of 20 seconds. This can be benign or progress to post-ictal asystole – fatal in 54% of cases. Careful attention should be paid to prodromal symptoms suggestive of focal seizures (including “auras”) in patients presenting with what might otherwise sound like syncope. These patients may have epilepsy presenting with ictal asystole and require antiepileptic drugs alongside their cardiac investigations/interventions.

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**Poster session THUR, 052**
Epilepsy in the land of ice and fire

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**Background:** Epilepsy is often explained through allegory; from magical thinking to misfiring neurons. It is important to appreciate pervasive media portrayals which influence lay attitudes toward epilepsy. George R. R. Martin’s series of fantasy novels A Song of Ice and Fire, and the HBO television adaptation A Game of Thrones, introduce characters with ‘mundane’ and ‘mystical’ epilepsy to millions. Cases are presented to highlight these varying portrayals.

**Cases:** RA, 8 years old, has “shaking sickness”. Triggered by stress, his hands “shake” with subsequent involvement of all limbs. He loses consciousness, is incontinent of urine, and demonstrates post-ictal confusion. He is enmeshed with his mother and his condition is viewed as a manifestation of his unsuitability to rule. BS fell at 9 years old, resulting in a coma. Subsequently he remains paraplegic with dialeptic episodes. During absences, he can ‘possess’ animals or people, and experiences impossible hallucinations. These abilities are portrayed as empowering for a boy who suffers heavy stigma against physical disability.

**Conclusion:** Fans will probably not adopt ‘magical’ views but may internalise stigma weighed against characters with both ‘mundane’ and ‘magical’ epilepsy. Due to the large audience, clinicians working with epilepsy patients might benefit from awareness of these portrayals.

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**Poster session THUR, 054**
The heart holds answers the brain cannot to see

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Neuronal ceroid lipofuscinosis (NCL) is a range of inherited lysosomal storage disorders. This case highlights the cardiac pathology associated with NCL and reports improved seizure control following correction of cardiac arrhythmias.
A 26-year-old woman presented with episodes of altered awareness with head and eye deviation on a background of a progressive neurodegenerative disorder. She initially presented at 7 years of age with progressive retinal dystrophy. As a teenager she developed seizures with prominent myoclonus, psychosis, cognitive impairment and immobility. Her epilepsy was refractory to treatment and seizures had increased in frequency prior to admission.

ECG demonstrated sinus bradycardia of 30bpm and episodes of 20sec sinus arrest. This was managed by the insertion of a pacemaker, resulting in a dramatic reduction in the frequency of her seizures. Investigation into the underlying disorder was revisited identifying vacuolated lymphocytes and homozygous CLN3 gene deletions. These findings are consistent with a diagnosis of juvenile NCL (Batten disease).

This case demonstrates the importance of cardiac monitoring in investigating a change in seizure pattern. We hypothesise that the patient presented with reflex hypoxic seizures secondary to asystolic episodes. It also highlights the value of securing a diagnosis to enable appropriate cardiac screening in NCL patients.

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**Poster session THUR, 056**

Juvenile myoclonic epilepsy in a tertiary centre - a database review

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**Background:** Juvenile myoclonic epilepsy (JME) is generally thought to respond well to first line treatment but many patients continue to suffer with seizure activity. This study reviews JME patients managed in a tertiary epilepsy centre.

**Methods:** A JME patient cohort with data on medication and seizure frequency was sourced from an epilepsy database at University Hospital of Wales, Cardiff.

**Results:** 168 patients (18-84 years old) were identified with a diagnosis of JME and a clinic appointment in the past 5 years. There was a female predominance of 2.8:1. The average age at onset was 13.

56% patients were free of generalised tonic-clonic seizures with 40% free of all seizure types. Of those with frequent seizure activity, 66% were on at least 2 anti-epileptic drugs (AEDs). Levetiracetam was the most common therapy (48%). 32 women of childbearing age (32%) were taking Valproate with 71% under regular follow-up.

**Conclusion:** Whilst JME is considered to respond well to AEDs a significant proportion in our tertiary cohort were deemed drug refractory. However, this may show bias when compared to community samples. The number of women taking Valproate highlights the benefit of the drug and the need for careful monitoring and shared clinical decision making.

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**Poster session THUR, 058**

Eslicarbazepine acetate as monotherapy in clinical practice

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Purpose: To assess eslicarbazepine acetate (ESL) as monotherapy in everyday clinical practice.

Method: Euro-Esli was a pooled analysis of 14 European studies. In a subanalysis, data were compared for patients treated initially with ESL monotherapy versus adjunctive therapy, and for patients treated at last visit with ESL monotherapy versus adjunctive therapy.

Assessments included responder rate (≥50% seizure frequency reduction), seizure freedom rate (seizure freedom at least since prior visit) and incidence of adverse events (AEs).

Results: ESL was used as monotherapy in 88/2045 and 229/1340 patients initially and at last visit, respectively. At 12 months, responder and seizure freedom rates were significantly higher in patients treated initially with ESL monotherapy versus adjunctive therapy (responder: 94.1% versus 74.8%; seizure freedom: 88.2% versus 39.0%), and in patients treated at last visit with ESL monotherapy versus adjunctive therapy (responder: 93.2% versus 70.4%; seizure freedom: 77.4% versus 25.9%). Overall incidence of AEs was similar in patients treated initially with ESL monotherapy and adjunctive therapy (29.4% versus 34.4%), and in patients treated at last visit with ESL monotherapy and adjunctive therapy (27.1% versus 30.8%).

Conclusion: ESL was significantly more effective when used as monotherapy compared with adjunctive therapy; safety/tolerability was generally comparable.

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Poster session WED, 061

'Real life’ experience with brivaracetam as add-on treatment for epilepsy

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Background: Brivaracetam received its UK licence as an adjuvant drug for focal epilepsy in adults in 2016. There is little data on its efficacy and tolerability in ‘real life’ settings. We present an interim analysis of a multicentre service evaluation of brivaracetam.

Methods: Data was retrospectively collected from clinical records at two UK centres of consecutive patients treated with brivaracetam and at least one follow up. Data were also extracted on previous levetiracetam use. Seizure frequency was categorised at baseline and follow-up (daily/weekly/monthly/yearly/none). Results: Of the 44 patients identified (17 male, mean age 39, range 19-66), 75% had a history of levetiracetam exposure (LE+) and 25% did not (LE-). Mean brivaracetam exposure was 10.3 months (2-21), the mean daily dose was 200mg (50-400). Retention was 91% vs. 100% in LE+ versus LE- groups at 3 months and 82% in both groups at 6 months. Seizure category improvements were seen in 20% / 36.4% in the LE+ vs. LE- groups, seizure category deteriorations in 0% vs. 9%. There were no serious adverse events.

Conclusion: Brivaracetam emerges as a potentially useful adjuvant medication for focal epilepsy. It may be better tolerated by some patients than Levetiracetam and more effective than this drug.

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**Poster session WED, 063**

Eslicarbazepine acetate switch from carbamazepine or oxcarbazepine

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Purpose: To investigate eslicarbazepine acetate (ESL) in patients transitioning from carbamazepine or oxcarbazepine in clinical practice.

Method: Euro-Esli was a pooled analysis of 14 European studies. Data were analysed for patients transitioning from carbamazepine and oxcarbazepine to ESL due to lack of efficacy or poor tolerability. Responder rate (≥50% seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit) were assessed after 3, 6 and 12 months of ESL treatment, and at last visit. Safety/tolerability analysis evaluated adverse events (AEs) and ESL discontinuation due to AEs.

Results: Euro-Esli included 2058 patients; 233 (11.3%) transitioned from carbamazepine and 134 (6.5%) transitioned from oxcarbazepine. After 12 months, responder and seizure freedom rates for patients transitioning from carbamazepine due to lack of efficacy (n=163) were 70.0% and 30.9%, respectively. Corresponding values for patients transitioning from oxcarbazepine due to lack of efficacy (n=90) were 57.1% and 25.0%, respectively. Among patients who transitioned from carbamazepine (n=64) and oxcarbazepine (n=61) due to poor tolerability, 26.6% and 39.5% experienced AEs; 8.3% and 6.8% discontinued ESL due to AEs, respectively.

Conclusion: ESL may be a useful option for patients experiencing intolerable AEs or not achieving adequate control with carbamazepine or oxcarbazepine.

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**Poster session WED, 066**

Web-based media as a self-management tool for people with epilepsy

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Background: There is little evidence on how people with epilepsy (PWE) use web-based media in self-management of their condition. This study focused on the benefits/risks for PWE using social networking sites and web-based media.

Methods: We recruited 14 PWE who had volunteered after seeing information provided by Epilepsy Action, UK. We asked open-ended questions about online media use. Interviews lasted 60-90 minutes. Sessions were recorded, transcribed, and thematically analysed using Nvivo.

Results: Seven men and seven women participated, age range: 33-73, average diagnosis length was 25 years. Twelve participants used web-based media to gather information
about their epilepsy. Seven used apps to manage their epilepsy by logging seizures or medication reminders. Six participants were hesitant to use web-based media due to privacy concerns. Four participants felt that epilepsy was underrepresented or misrepresented online. Three participants preferred traditional sources of epilepsy-related information.

Discussion: Results show the value of web-based media in providing information and support to PWE, with the caveat that concerns around privacy and disclosure can undermine potential benefits. Health service providers and advocacy groups can assist by ensuring online information is accurate and up-to-date. Further research may help in developing understanding and future services.

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**Poster session THUR, 071**
Towards an integrated tool for PNES assessment
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Introduction: Psychogenic non-epileptic seizures (PNES) can present a real diagnostic challenge, with subsequent impact on the course of the disorder and its management. A number of studies have looked into predictive factors for PNES. However, no guidance is available for applying the findings of these studies in clinical practice.

Aim: The aim is to combine the most recognised discriminative features into an integrated clinical tool, ultimately, to improve the predictive value of the medical assessment of patients with possible PNES in a clinic setting. This can be invaluable in centres with limited access to video telemetry (VT).

Methods: The following criteria were employed and compared with the results of VT as gold standard:
- Patient comorbidities
- Conversation analysis
- Review of system questionnaire
- Ictal semiology and autonomic activation
- Postictal prolactin and lactate

Results and conclusion: This QIP will assess the reliability and validity of various criteria in recognising PNES clinically. Based on our findings, an integrated tool will then be designed as an adjunct to the standard medical assessment in settings where VT is not readily available.

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**Poster session THUR, 075**
Evaluating a personal information pack in epilepsy
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Abstract: A mainstay of epilepsy management is patient education and engagement. Previous educational interventions have varied greatly in number of sessions, teaching
methodology and cost. This study assessed the impact of a low-cost intervention consisting of a personal information pack.

Methods: Forty-six consecutive patients with an existing epilepsy diagnosis attending clinic at MKUH NHS Trust were enrolled and pack provided. A baseline questionnaire assessed patient understanding and service utilisation (GP, A&E, specialist nurse). The questionnaire was repeated 3 months later. Patient engagement with the pack was assessed (completeness of information in pack, patient rating of usefulness).

Results: Fourteen patients were lost to follow-up - thirty-two completed the second interview. There was a trend towards reduced service utilisation. Specialist nurse visits were significantly reduced (2.75 visits/year pre-intervention vs. 1.11 post-intervention, p=0.01). Patient understanding was not significantly changed. Patient rating of usefulness was positive (2.4/3 on Likert scale). Two thirds of patients had not filled out the pack or added basic details only.

Discussion: This simple, low cost intervention may reduce some types of service utilisation and be found helpful by patients. A planned redesign involves the provision of a low-effort pre-filled information card together with the larger pack.

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**Poster session WED, 078**

‘Not just a headache’: social media use in people with migraine

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Introduction: ‘Invisible’ conditions like migraine may leave individuals seeking support and information. We aimed to describe how people with migraines use and benefit from social media and to identify harms of social media use.

Methods: Twenty participants were recruited via migraine charities. Semi-structured interviews were conducted with questions based on a topic guide. Interviews were transcribed and analysed using thematic analysis.

Results: We found people with migraine use social media to better understand their condition and treatment options. It offers instant access to continuous information and social support from empathic others. Participants viewed social media as an outlet to vent frustrations and to validate their migraine experience. They referred to the invisible and episodic nature of migraine which contributes to misunderstanding of the impact and/or severity of the condition. Some masked their online migraine-related behaviour, using different sites or closed online groups, which sometimes changed their online behaviour in other areas. Harms of social media included inaccuracy of information, occasional negativity, and privacy issues.

Conclusions: Social media can provide people who experience migraines with instant, continuous access to social support and health information, from empathic others. This can validate their illness experience, reassure and help to reduce feelings of isolation.

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**Poster session WED, 079**

Epidural blood patch: impact of non-Luer one-way butterfly needle
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The epidural blood patch (EBP) requires a syringe that connects to the intravenous and epidural route. Thereby contravening Department of Health guidance, which recommends adoption of equipment that, prevents wrong route drug administration. To comply with these recommendations a non-Luer butterfly needle with one-way valve has been produced by GBUK. The one-way valve and length of tubing has the potential of activating the clotting cascade. This could reduce the time clinicians have to utilise the blood in the syringe. Also any alteration in clotting could affect the therapeutic value of the EBP. The primary objective of this research was to determine if phlebotomy using this new 21G needle altered blood clotting, determined by thromboelastograph analysis, compared to a standard 21G hypodermic needle.

We performed paired phlebotomy on 10 healthy volunteers; producing a study capable of revealing a 25% change in R-time (power 80%). Mean R-time was increased with the new needle, however remaining within normal range (7.3 vs 6.6 minutes (p=0.04)). This would not limit the time to utilise the blood before clot formation in the syringe. With no clinically relevant difference in MA or LY30, it is unlikely to have any impact on the therapeutic value of the EBP.

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**Poster session WED, 080**

Experiences of specialist referral and GP access to MRI for headache

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Introduction: When General Practitioners (GPs) refer patients with headache to neurologists, it is often because the patient and/or doctor want imaging. Some GPs now access Magnetic Resonance Imaging (MRI) directly. We aimed to describe patients’ experience of GPs using direct access, compared to patients who saw a specialist first.

Methods: We invited participants to semi-structured Interviews about two months after imaging. Interviews were audio-recorded, transcribed, and analysed using thematic analysis in Nvivo.

Results: We interviewed 10 patients from each pathway in South London, eleven women, median age 41, range 20-72. We found more similarities than differences between groups. Ten said they received a clear scan result explanation, while six had difficulty understanding results. Eleven participants felt relief once results were received, while five still wanted an answer on the underlying cause for symptoms. Seven felt the specialist appointment wait time was long. Those using the direct-access pathway were more likely to report MRI results delay.

Conclusion: Patient reassurance was linked closely with results receipt and worry linked with wait times. Some felt MRI results did not provide sufficient explanation for symptoms. Improvement in both pathways can be achieved, providing results are delivered in a clear, timely manner.

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**Poster session THUR, 084**

Cranial autonomic symptoms in cluster headache induced by nitroglycerin

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**Introduction:** Cluster headache (CH) is characterised by attacks of unilateral excruciating headache, ipsilateral cranial autonomic symptoms (CAS) and/or agitation. Studying of CAS can further our understanding of CH pathophysiology, but is limited by the episodic nature of the disease. Nitroglycerin (NTG) is known to induce CH. The aim of this study is to characterise CAS induced by NTG.

**Methods:** CH patients received intravenous NTG 0.5mcg/kg/min over 20 minutes. CAS and headache phenotype were recorded. The study was approved by the NHS Research Ethics Committee.

**Results:** Twenty-three patients participated: 83% male and 61% episodic cluster headache. The most common spontaneous CAS reported were lacrimation, nasal congestion and conjunctival injection. Agitation was reported in 96%. Nitroglycerin induced ipsilateral CAS in 91% of the patients, with 74% with ipsilateral pain. Most commonly induced CAS were nasal congestion, lacrimation and periorbital swelling. Agitation was reported in 61%. The majority of the CAS (80%) induced by NTG presented before the onset of severe pain.

**Conclusion:** We demonstrate that NTG effectively triggers ipsilateral cranial autonomic symptoms in CH patients and that they often present in a phase before the onset of pain reflecting the underlying pathways during a cluster headache attack.

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**Poster session THUR, 090**

Idiopathic intracranial hypertension – towards a streamlined pathway

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Recent studies have yielded the first evidence-based treatments for idiopathic intracranial hypertension (IIH) and shed light on many aspects of this condition, providing an opportunity to streamline the assessment and management of patients with IIH.

This study highlighted the inefficiency of most patient pathways, especially when via outpatients, with resulting delays in diagnosis & management. Of note, 37% of patients did not have venography. Up to a third of patients with cerebral venous sinus thrombosis present with isolated signs of elevated intracranial pressure, thus clinically mimicking IIH and emphasising the importance of venography acutely.

Acetazolamide was appropriately commenced but rarely titrated to the maximum dose of 4g/day as supported by the IIHTT. Over 40% of our cohort had a diagnosable co-morbid primary headache disorder which persisted and required additional headache-specific medication in almost half of these. This is in keeping with studies showing that headache is unrelated to raised intracranial pressure in IIH patients, and headache-specific management is a key aspect to the management of IIH patients.
In summary, this study highlights significant delays and missed investigations when not performed acutely, emphasising the importance of implementing a clear and visible pathway for the assessment and management of IIH patients.

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**Poster session WED, 094**
Diagnostic error rates in diagnosing idiopathic intracranial hypertension

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Objective: To quantify the rate of diagnostic error amongst patients with IIH. Additionally to identify factors contributing to diagnostic error.

Methods: Sequential patients referred with a diagnosis of IIH to the Birmingham tertiary neuro-ophthalmology IIH clinic were prospectively included (October 2013-February 2017). A diagnostic error taxonomy tool was applied to cases referred as “definite” or “possible” IIH. Discrepancy between referred and final diagnosis were recorded.

Results: 212 patients were referred, (96.2% female), 138/212 (65%) with definite IIH and 74/212 (35%) with possible IIH. Of those diagnosed with definite IIH 25% were not IIH and out of those diagnosed with possible IIH 57% were not IIH. Reasons for diagnostic error included incorrectly identifying papilloedema where in fact pseudopapilloedema existed and diagnosing IIH following an isolated lumbar puncture (LP) pressure >25 cmCSF (but in the absence of other diagnostic criteria for IIH). Misdiagnosis lead to 43% receiving unnecessary acetazolamide (or other diuretics) and 14% having multiple LPs.

Conclusions: We noted a high diagnostic error rate amongst IIH patients referred to a tertiary centre for ongoing management. Where there is doubt about the presence of true papilloedema early specialist review may reduce unnecessary treatment and LP’s.

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**Poster session WED, 097**
Diagnostic lumbar punctures in IIH: what is the patient experience?

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Aims & Methods: Patients with idiopathic intracranial hypertension (IIH) often report significant morbidity associated with lumbar punctures. We therefore aimed to assess the patient’s experience of diagnostic lumbar puncture (LP) in IIH using an online survey designed in collaboration with IIH:UK (a leading UK charity).

Results: 463 patients responded to the survey, and were eligible for analysis, over a 2 month period in 2015. 40% of patients described severe pain during the LP (VRS ≥8), and the median pain score during the LP was 7 (VRS, IQR 5-7). The majority of patients felt they received insufficient pain relief (85%). Levels of anxiety about future LP’s were high (median VRS 7, IQR 4-10), with 47% being extremely anxious (VRS ≥8). LPs performed as an emergency were associated with significantly greater pain scores compared to elective procedures (median 7, IQR 5-7 vs. 6, IQR 4-8, p=0.012). Higher LP pain scores (VRS) were significantly associated with poorly informed patients (Spearman correlation, r=-0.32, p<0.001).

Conclusions: This study has shown that a significant number of these patients are experiencing significant morbidity from pain and anxiety. This morbidity is associated with both inadequate pre-procedural information, as well as the setting the LP is performed in.

Poster session THUR, 101

SCA-1 with unusual early dysautonomia and delayed cerebellar signs

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A 59-year-old right-handed bus driver presented with gradually worsening erectile dysfunction, urinary frequency and nocturia over 18 months. He had a past medical history of hypertension with regular medications including amlodipine, aspirin and atorvastatin. Initial examination revealed a mild bilateral intention tremor. The patient had undergone brain imaging showing brainstem and cerebellar atrophy with a “hot cross bun sign”. The patient was then referred for autonomic function tests that demonstrated mild cardiovascular autonomic changes, and suggested sympathetic dysfunction. A working diagnosis of multiple system atrophy (MSA) was made.

Over the next two years, his tremor worsened with the development of slurred speech and unsteady gait. On examination, he had prominent fasciculations and wasting in the right shoulder, severe bilateral intention tremor with past-pointing. In addition he had Parkinsonism and signs of a sensorimotor neuropathy. This atypical clinical evolution with prominent neuropathy and cerebellar signs led to investigations for spinocerebellar ataxia (SCA), particularly type 2 or 3 (given the autonomic dysfunction). However, the genetic testing showed a mutation in ATXN1, confirming a diagnosis of SCA type 1.
To our knowledge, this is the first reported case of prominent early autonomic dysfunction associated with SCA type 1.

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**Poster session THUR, 103**
Chorea associated with atrial myxoma

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Background: Chorea is a hyperkinetic movement disorder characterised by involuntary, unpredictable muscle contractions and is associated with a broad range of primary and secondary aetiologies.

Case: A 73-year-old gentleman presented with a 12-month history of progressive behavioural change and involuntary movements. His family had become concerned about periods of erratic behaviour and confusion. He appeared agitated and restless. On examination he had choreiform movements predominantly affecting his upper limbs. An abnormal diastolic heart sound was detected on auscultation.

MRI brain and CSF analysis were normal; ASO titre, paraneoplastic, anti-NMDAr antibodies and Huntington’s genetics were negative. A blood film was normal. Transoesophageal echocardiogram demonstrated a variegated mobile mass within the left atrium.

An immune-mediated mechanism was suspected. Intravenous immunoglobulins and oral corticosteroids were trialled with initial major benefit but he relapsed several months later and did not respond to a further trial. The atrial mass was resected and histological analysis confirmed an atrial myxoma. The chorea and cognitive symptoms significantly improved after surgery and he remains well.

Discussion: Atrial myxoma is the most common primary tumour of the heart and is rare with an incidence of 0.5/1,000,000 population/year. There has only been one other case in the paediatric literature.

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**Poster session THUR, 104**
Global MD registry and dystonia non-motor symptoms study

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Myoclonus Dystonia (MD) is a rare hyperkinetic movement disorder with an early childhood onset. Estimates of MD prevalence among European populations places this at 1 in 500,000 individuals, however no worldwide estimates currently exist. MD patients experience alcohol-responsive myoclonus predominantly affecting the trunk and upper limbs, and dystonic posturing typically involving the neck and hands (writer’s cramp) but may also involve other parts of the body (e.g. lower limbs and trunk). Individuals with MD also frequently report non-motor symptoms (NMS) such as psychiatric co-morbidity, significant pain that impacts function and daily living, and disturbance to sleep.

This study aims to develop a global register of MD patients of all ages, and further characterise the NMS in 500 adult MD patients via validated online psychiatric, sleep and
pain questionnaires and cognitive tests. The register will also be used to establish a research hub to direct future research into elucidating disease mechanisms, and develop novel therapeutic targets for MD. The online questionnaires will be developed using the Bristol Online Surveys platform. All data will be encrypted to ensure patient confidentiality, and then analysed using Microsoft Excel and R statistical software package. P values less than 0.05 will be deemed as statistically significant.

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**Poster session WED, 106**

Unilateral abnormal DaT scan: early indicator of Parkinson’s disease

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Introduction: Dopamine transporter (DaT) scans are used in the investigation of clinically uncertain Parkinsonian syndromes (CUPS). Presently, bilateral abnormal DaT scans are diagnostic of Parkinson’s disease and degenerative Parkinsonism, while normal scans suggest non-degenerative causes. However, the clinical significance of unilateral abnormal scans remains ambiguous. Therefore, we aimed to determine their relevance in CUPS, and hypothesised that they may presage Parkinson’s disease and degenerative Parkinsonism.

Methods: A retrospective analysis was performed for patients with CUPS within a tertiary institution who had undergone DaT scans. Demographic data, clinical features, imaging and diagnoses were collected. In patients with unilateral scans, follow-up assessments, further imaging and diagnostic changes were also recorded.

Results: A total of 200 DaT scans were performed from 1 January 2008 to 1 January 2017. There were 100 (50.0%) with normal scans, 77 (38.5%) with bilateral scans, and 23 (11.5%) with unilateral scans. Of the latter group (N=23), 8 (34.8%) underwent follow-up DaT imaging in a mean period of 31.9±12.6 months from baseline, with 4 (17.4%) now reported as bilateral, although 2 (8.7%) remained unilateral and 2 (8.7%) were reported as normal.

Conclusion: Unilateral DaT scans can serve as a predictive factor for development of Parkinson’s disease and degenerative Parkinsonism.

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**Poster session WED, 109**

Computer vision: a smartphone camera can ‘see’ bradykinesia

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The core clinical feature of Parkinson’s disease is bradykinesia. However, the most common method of clinical assessment, finger tapping, has poor inter-rater reliability, even among movement disorder specialists. Many technologies have been devised to objectively measure finger tapping, but virtually all involve specialised equipment, which may explain why none are in widespread use. One method involves patients tapping a
smartphone screen, but this cannot detect tapping amplitude or decrement (key features of bradykinesia assessment).

Computer vision takes static or moving images from a camera, and then applies computing algorithms to automatically extract useful information. It is widely used in commercial applications, such as facial detection and recognition of facial expression. Crucially, the only hardware required is a simple camera with a computer processor, and such items are ubiquitous, e.g. smartphones. We report a computing method, including the technique of ‘optical flow’, which uses video from a smartphone to detect the pixels of the hand and track their movement during finger tapping. It has the potential to detect and measure bradykinesia without the need for specialised equipment. We present striking videos and early results comparing computer vision measurements of finger tapping with clinical ratings for Parkinson’s patients and controls.

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**Poster session WED, 112**

Seeing invisible Parkinsonian tremor with a smartphone camera

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Arthur C Clarke’s ‘third law’ states that any sufficiently advanced technology is indistinguishable from magic. Computer vision is the processing of images or video by computer to extract useful information. A technique termed ‘Eulerian magnification’ involves amplification of tiny movements from video recordings, so that very small motions can become visible to the human eye. This has the potential to detect tremor that is of such small amplitude it cannot otherwise be seen. Crucially, the only hardware required is a camera and computer processor, items that are ubiquitous. There is only one previous report of Eulerian magnification applied to a simple video of a Parkinson’s patient, but Parkinsonian signs could clearly be seen in the pre-processing video, and no control video was shown. We present remarkable video in which no tremor is seen in either patient or control before processing, and yet a Parkinsonian tremor is revealed in patient but not control after amplification. Blinded clinician ratings detect a greater number of Parkinsonian tremors after computer processing. Furthermore, we report a method using an ‘optical flow’ computing technique that records pixel motion vectors, and enables the computer to measure the direction and relative amplitude of this amplified movement.

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**Poster session WED, 114**

Pathways to diagnosis in PSP, CBD and PD

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Misdiagnosis and delayed diagnosis are common in PSP/CBD. To inform approaches to reduce diagnostic delay, it is essential to systematically evaluate patient pathways to diagnosis.

Cases with a final diagnosis of PSP (n=28), CBD (n=2), and 30 age-sex matched PD controls, were identified from the Parkinsonism Incidence in North-East Scotland study. Using general practitioner, hospital and research records, referral and diagnostic time intervals from symptom onset to death were recorded.

Comparing PSP/CBD to PD, the median (interquartile range) time intervals from index symptom to first secondary care referral [0.7(0.01,2.53) vs 0.02(0.00,0.73) years] and review [0.84(0.18,2.56) vs 0.03(0.07,0.88) years], and, first neurologist referral [1.67(0.70,4.45) vs 0.12(0.00,1.56) years] and review [1.72(0.88,4.53) vs 0.23(0.11,1.65) years], were significantly longer in PSP/CBD (p=0.001 to 0.031). The average time intervals from index symptom to a parkinsonian syndrome diagnosis [2.26(0.85,5.41) vs 0.10(0.00,0.90) years], inclusion of the final diagnosis amongst differential diagnoses [3.62(2.06,7.21) vs 0.16(0.00,1.53) years], and the final diagnosis as primary diagnosis [4.22(2.28,7.63) years vs 0.67(0.10,3.04) years] were similarly longer in PSP/CBD (p=<0.001).

Referral and diagnostic time intervals are significantly longer in PSP/CBD when compared to PD. Identifying factors that both improve the timing and destination of referral decision-making, and the accuracy and timeliness of diagnosis is necessary.

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Poster session THUR, 117

The L-dopa response in pathologically confirmed Parkinson’s disease

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Background: L-dopa is the standard treatment for Parkinson’s disease, but the response is variable.

Aim: Systematic review of papers reporting the L-dopa response (motor response and/or complications) in pathologically confirmed Parkinson’s disease.

Results: 467 cases of pathologically confirmed Parkinson’s were identified: 60.2% male, age at disease onset 63.3 years (SD 10.3), age at death 76.7 years (SD 7.8). Data on a graded L-dopa response were available in 411 cases (88.0% of 467). The motor response was excellent in 148/411 cases (36.0%), good in 179/411 (43.6%), moderate in 51/411 (12.4%) and poor/absent in 33/411 (8.0%). Data about motor complications were available for 161 patients: 71/161 (44.1%) had motor fluctuations and 89/161 (55.3%) had dyskinesia. Comorbid brain pathology was evaluated in 251/411 cases (61.1%), and
was present in 148/251 (59.0%): cerebrovascular in 65/148 (43.9%), Alzheimer’s in 55/148 (37.2%), amyloid angiopathy in 18/148 (12.2%), and diffuse Lewy body disease in 10/148 (6.8%). Data linking the graded L-dopa response to comorbid pathologies were available in only 17 cases, of whom 8/17 (47.1%) had a good/excellent response.

Conclusion: There is variation in the L-dopa response in pathologically confirmed Parkinson’s disease. The limited available information suggests a possible association of motor response to comorbid brain pathology.

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**Poster session THUR, 120**

Postprandial hypotension in MSA and PD with autonomic failure

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Introduction: Postprandial hypotension is often reported in Parkinson’s disease with autonomic failure (PD+AF) and Multiple System Atrophy (MSA). However there has been no study directly comparing this feature between these two disorders. The aim of this study was to evaluate cardiovascular autonomic responses before and after standard liquid meal ingestion in PD+AF and MSA.

Methods: Patients underwent a liquid meal challenge using a previously described protocol. Blood pressure (BP) and heart rate (HR) were measured at intervals. All participants remained supine for 45 minutes after the liquid meal ingestion. They underwent 10-minute head-up tilt (HUT) to 60° before and 45 minutes after the meal.

Results: 22 MSA and 11 PD+AF patients were identified. Supine post-prandial hypotension was significantly more common in PD+AF compared to MSA (73% vs 36%; p<0.05). Both groups had orthostatic hypotension during pre-meal tilt, with no significant difference in BP and HR when tilted post-meal between PD+AF and MSA (p>0.05).

Conclusion: Despite the similar degree of orthostatic hypotension on supine and HUT, postprandial hypotension is more commonly present in patients with PD+AF compared to MSA. The increased tendency to post-prandial hypotension even while supine reflects the nature of post-ganglionic sympathetic denervation in PD.

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**Poster session THUR, 121**

Identifying participants with Parkinson’s disease in UK Biobank


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Background: Linkage to routinely collected NHS data from primary, secondary care and death certificates enables identification of participants with Parkinson’s Disease (PD) within the UK Biobank cohort of 500,000 adults. Validation of the accuracy of this data is required prior to their use in research studies.

Method: In this validation study participants (n=125) with a code indicating PD were identified from a sample of 17,000 participants in the cohort. Diagnoses were validated by expert adjudicators, based on free text electronic medical records. Positive predictive values (PPV, % of cases identified that are true cases) were calculated.

Results: Primary care diagnostic codes identified 93% of PD cases, with a PPV of 95%. Combined secondary care and death data identified 42% of PD cases with a PPV of 84%. Combining diagnostic and medication codes identified more participants, but did not increase the PPV.

Conclusions: This study suggests that linkage to routinely collected healthcare data is a reliable method for identifying participants with PD in the UK Biobank cohort.

Primary care diagnostic codes identified the highest proportion of participants and had the highest PPV, demonstrating the value of using primary care data to identify cases of disease in large population based cohort studies.

 Poster session THUR, 122

Parkinson’s KinetiGraph improves movement disorder service provision

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Introduction: Objective evaluation of symptoms of Parkinson’s disease (PD) can be challenging. There is increasing interest in technological solutions to assess, monitor and manage people with PD.

Objective: To evaluate the effect of the Parkinson’s Kinetigraph (PKG) on management of patients with PD in a large tertiary movement disorder service.

Methods: We retrospectively reviewed the notes of 47 patients with PD (22 female, 25 male) who underwent PKG recording over a six month period. The indications and PKG findings, and the subsequent effect on clinical decision making and service provision were recorded.

Results: Management was significantly altered in 25 patients (53%), while in 13 patients (28%) PKG confirmed the use of advanced therapies such as deep brain stimulation. Significant effects were seen with regard to service provision. Outpatient appointments could be deferred with advice following PKG in 15 (32%), advanced therapies assessment was improved in 16 (34%), while inpatient admission was avoided in six patients (13%).

Conclusion: The use of PKG has enhanced service provision in our movement disorder service. In particular, it enhances our assessment of patients considered for high-cost advanced therapies, allows more efficient use of clinic appointments, and has the potential to reduce hospital admissions.

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 Poster session WED, 127
Update on the Questionnaire for Brain Donors at Queen Square Brain Bank

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The Queen Square Brain Bank (QSBB) is recognised as a world leading neuropathological resource for brain tissue for study into Parkinson's disease (PD) and Parkinson-plus syndromes. At recruitment to the donor register, a self-assessment form is given to every donor and used for administrative and research purposes. Due to the recent increase in donations from individuals with Parkinsonian syndromes and the latest advances on risk factors and symptomatology of PD, a new questionnaire is needed. This study is a literature review of existing self-report questionnaires used in PD, Parkinson-plus syndromes, hyperkinetic disorders and cognitive impairment, to assess their suitability for inclusion in the new questionnaire for QSBB brain donors. This is the first systematic review of our knowledge to include all five domains of Parkinsonian symptoms. Subsequently, the modified Delphi method was used to reach a consensus of the domains from an expert panel. This information was cross-referenced with the Clinical Data Interchange Standards Consortium. Through the creation of this new questionnaire, we hope to improve the quality of the data collected from brain donors, which hopefully will ultimately help improve our understanding and management of these disorders.

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Poster session WED, 128

Care and unmet needs in Late-stage Parkinsonism: A qualitative study

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Aim: To explore experiences and views about care needs and service use by people with late-stage Parkinsonism.

Method: Ten participants at Hoehn and Yahr stage 4 or 5 were interviewed using semi-structured open ended questions and qualitative content analysis.

Findings: Despite severe disability, participants expressed their desire to maintain normality of activities and interests in their lives. Many perceived that even though health care was provided by professionals they could do nothing more for them. Participants experienced having to 'fit-in' to service structures that did not always accommodate their complex needs. The quality of relationships with health care professionals and formal carers shaped perception of service provision and mediated adaptation. Informal support and knowledge on disease management were key factors in their perceived ability to remain in control and to enable normal functioning. There was common reluctance to discuss, and uncertainty about, future plans. For example, moving to a residential nursing home was perceived an undesirable but potentially necessary only option for future care.
Conclusion: Addressing these findings including greater flexibility of healthcare structures and better future planning could increase ability of patients with late-stage parkinsonism to remain at home and improve quality of life of patients in this late disease stage.

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Poster session WED, 129
Improving Community Exercise Provision in Parkinson’s

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Objective: To improve community-based exercise provision for people with Parkinson’s (PwP).

Background: Regular exercise of moderate-high intensity is beneficial to PwP, significantly reducing impact of symptoms and improving quality of life.

Aim:

To increase exercise opportunity for PwP by:

1) Development, delivery and evaluation of a programme to increase community exercise providers’ knowledge and understanding of Parkinson’s disease (PD).

2) Development of a ‘tool kit’ to facilitate national dissemination of the course.

Methods:

Funding was achieved from Active Devon and Parkinson’s UK. Course content and evaluation methodology were developed by the PenPEN training co-ordinator (VE), and project team. The 3-hr pilot course was delivered in November 2017. A pre- and post-course questionnaire was administered to participants.

Results: 25 Delegates attended the course, representing a range of activities including dance, swimming and football. 100% completed questionnaires. Evaluation demonstrated significant improvement in comfort communicating with PwP ($p=.002$), understanding of PD and the benefits of exercise, and suggesting exercise to PwP ($p<.001$).

Conclusions: We have developed a means of increasing community exercise provision for PwP. Details of trained exercise providers are disseminated via clinics and Parkinson’s UK branches. An Exercise Provider Training Toolkit will be made available via the Parkinson’s Excellence Network.

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Poster session WED, 130
Designing a Care Pathway for High Risk Parkinson’s Patients
Objective: To inform pathway design for patients at high risk of an adverse outcome at 5 years post-Parkinson’s disease (PD) diagnosis.

Background: In our service, all newly diagnosed patients follow a 12-month new patient pathway, which includes assessment with PDQ-39, NMS Quest and MOCA. Use of a prognostic calculator allows for refinement of the pathway according to patient need. Patients are classified as low (0-0.3), medium (0.31-0.79) or high (0.8-1) risk of an adverse outcome at 5 years (postural instability, dementia, death).

Aim: We aim to evaluate whether assessments in the newly diagnosed pathway identify additional care needs in higher risk patients.

Methods: An evaluation was carried out of our new patient database. Individuals who had the prognostic indicator performed (n=52) were included in the evaluation.

Results: Patients in the high risk groups were found to be older and more cognitively impaired than lower risk patients (p<.05). MOCA scores negatively correlated with NMS Quest (r=-.44, p<.001) and PDQ-39 (r=-.51, p<.001) suggesting as cognition becomes impaired, NMS burden increases, and quality of life is reduced.

Conclusions: Additional care needs were identified in high-risk patients. These findings highlight additional resources are required in this patient cohort to ensure needs are met.

References:

Poster session WED, 131
Evaluating the clinical utility of the Parkinson’s KinetiGraph (PKG)

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Objective: To evaluate the utility of the Parkinson’s Kinetigraph (PKG™) in the remote management of Parkinson’s disease (PD).

Background: There is a movement in Parkinson’s care from a clinic-based model (1) to P4 medicine, meaning medicine that is predictive, preventive, personalised and participatory (2). The development of wearable technology provides an opportunity to monitor patients remotely, and deliver targeted care. The PKG™ is a wrist-worn device that objectively measures Parkinson’s symptoms.

Aim: To evaluate the utility of the PKG™ in managing PD patients remotely, and the perception of service users.
Method: PKG™ data were collated in real time. Patient acceptability data were collated via a patient questionnaire (n=61).

Results: Between July 2015 and January 2018, 216 PKGs were performed. A variety of symptoms were identified, including different types of ‘OFF’ times (wearing off (25%), delayed on (6%) no drug response (8%)) and non-motor complications (fragmented sleep (33%) and daytime somnolence (21%)), with subsequent treatment recommendations being made. Patient acceptability of the PKG™ was high, 81% of patients being satisfied not having to travel for clinic appointments.

Conclusions: The PKG™ facilitated remote treatment recommendations. Remote management was acceptable to patients. Future evaluations will evaluate patient outcome.

References:


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Poster session THUR, 132

Neuroschistosomiasis: complication of a neglected tropical disease

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Neuroschistosomiasis is an under-recognised complication of one of the world’s most prevalent, yet neglected parasitic diseases, which if left untreated can result in severe disability. Although schistosomiasis is most commonly found in the tropics, neurologists in developed countries must have a low index of suspicion in the appropriate clinical setting.

We describe a 17 year old previously fit and well Guinean lady presenting with subacute, progressive, symmetric lower limb hyperaesthesia and urinary retention. Neurological examination was consistent with a myeloradiculopathy. Initial tests revealed an eosinophilia and raised ESR. CSF and imaging findings supported the clinical diagnosis of myeloradiculopathy secondary to schistosomiasis. She responded well to empirical steroids and praziquantel with complete resolution of sensory and urinary symptoms over several weeks. Serology later confirmed the diagnosis.

Transverse myelitis and myeloradiculopathy affecting the conus medullaris and/or cauda equina are the most common presentations associated with neuroschistosomiasis. Symptoms are principally due to an inflammatory response to the retained schistosome eggs. This case details the differential diagnosis of a subacute myeloradiculopathy and highlights the importance of a thorough travel history. In the appropriate clinical context,
neuroschistosomiasis should be included in the differential diagnosis of a subacute myeloradiculopathy, enabling prompt diagnosis and optimal management.
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**Poster session THUR, 134**

Isolated CNS histoplasmosis in an immunocompetent patient

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A 26-year-old Bolivian man presented with a 3-year history of occipital headaches and bilateral papilloedema. MRI showed communicating hydrocephalus and leptomeningeal enhancement. CSF analysis revealed an opening pressure of 32cmH₂O, lymphocytic pleocytosis, protein 1.9g/dL and CSF glucose 0.4 mmol/L. CSF AFB, bacterial and fungal culture, TB-PCR, 18S rDNA PCR, serum b-d glucan, and HIV were all negative. Serum ACE was normal. Steroids and methotrexate were commenced for probable neurosarcoidosis.

He had readmissions with recurrent headache, meningism, symptoms of raised intracranial pressure and development of limb spasticity and brisk reflexes. Repeat imaging demonstrated stable hydrocephalus. Despite immunosuppression and empirical TB treatment, he remained symptomatic with a persistently active CSF: maximum opening pressure 36cmH₂O, protein 3.9g/dL, WCC 205 lymphocytes and low CSF-to-serum glucose ratio on repeated therapeutic LPs.

After re-evaluation and positive CSF b-d glucan, a diagnosis of Histoplasma meningitis, without systemic dissemination, was confirmed by positive serological and CSF tests: positive immunodiffusion; yeast CFT 1:16; CSF EIA antigen 0.85ng/ml.

He was treated with AmBisome, followed by oral itraconazole, with complete symptom resolution and improvement on interval imaging.

We discuss challenges in reaching a diagnosis of isolated histoplasmosis, its neurological manifestations and diagnostic pathway in evaluating patients with suspected CNS fungal infection.

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**Poster session WED, 139**

Gene expression regulation in CD4+ T-cell dysfunction in MS

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Background: Genetic risk variants for complex disorders such as multiple sclerosis (MS) rarely encode protein. Growing evidence suggests risk variants regulate gene expression in specific disease-relevant cells by altering regulatory genetic sequences. This can be explored by correlating genotype at risk loci with expression of nearby genes (cis-regulation), with greatest sensitivity demonstrated in the most relevant cell types.
Identifying genes under regulation by the MS risk variants could be a crucial step in identifying novel therapeutic targets.

Aims: 1) Interrogate MS risk loci for cis-regulatory effects using allele-specific expression (ASE) analysis. 2) Establish a publicly available resource of genome-wide RNA-seq expression data in CSF-derived CD4+ T-lymphocytes. 3) Correlate gene expression data with longitudinal clinical data to seek biomarkers of prognosis.

Method and progress: We have extracted RNA from FACS-sorted CSF-derived CD4+ T-lymphocytes from over 100 individuals. cDNA library preparation and sequencing for each sample is underway.

Data analysis: ASE analysis makes use of a pre-selected transcribed SNP to differentiate maternal and paternal transcripts of each gene of interest. When an individual is heterozygous at an additional functional regulatory locus the ratio of maternal: paternal expression will deviate from 1:1. Each MS risk locus will be interrogated for this effect.

Poster session WED, 141
Pathological correlates of age at death in multiple sclerosis

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Introduction: Few studies have investigated which pathological features, including systemic vascular disease (VD), associate with younger age at death in multiple sclerosis (MS) and this constitutes the aim of the present study.

Methods: a post mortem MS brain autopsy tissue was studied for 1) systemic VD scores 2) % brain plaque area and activity from a) frontal plus occipital white matter (WM), b) pons, and c) basal ganglia (BG), 3) frontal plus occipital cortex. These pathology measures, sex, disease duration (DD), and cause of death, were fitted into a regression model to explain age at death.

Results: 34 MS cases (mean age 61.6 ±13.05 years, 58.8% females, DD 20.2±13.45 years) were included. Age at death decreased with increasing WM+pons+BG (r=- 0.382, r=0.02) and cortical (r=-0.299, p=0.03) demyelination, and WM+pons+BG active plaques (r=-0.326, p=0.011) but increased with DD(r=0.298, p=0.016) and VD(r=0.329, p<0.0001). In the regression model only cortical demyelination (b=-0.39, p=0.014), DD (b=0.36, p=0.009) and VD (b=0.64, p=0.001) persisted.

Conclusion: Higher cortical demyelination associated with younger age at death. Systemic VD did not associate with younger age at death in this MS cohort.

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Poster session WED, 142
‘Anti-Hu syndrome’ - a case of paraneoplastic sensory neuropathy with encephalitis

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A 75-year-old female was referred to the neurology outpatients department with a 6-month history of progressive amnesia and cognitive decline as well as symptoms/signs
suggestive of a sensory neuropathy. Past medical history included TIA, cervical spondylosis and recent investigation for hyponatraemia which had been attributed to SIADH. She had been a smoker with a 50+ pack year history and consumed minimal alcohol. An MRI brain scan demonstrated bilateral hippocampal T2 hyperintensity. A lumbar puncture demonstrated normal CSF constituents and negative viral PCRs. Full autoimmune and paraneoplastic screening was undertaken which was all normal except for a positive anti-Hu antibody. A CT-TAP highlighted a mass lesion in the right middle lobe of the lung and biopsy confirmed small cell lung cancer (T1aN2M0). A diagnosis of anti-Hu antibody related paraneoplastic syndrome was made and an initial treatment course of IV Methylprednisolone was administered. The patient’s cancer was treated with chemotherapy and adjuvant radiotherapy. Despite a good response with regard to her tumour and hyponatraemia, the patient did not improve significantly cognitively. This case highlights the need for awareness of the combination of symptoms/signs of the described “anti-Hu syndrome” with paraneoplastic sensory neuropathy and/or encephalomyelitis.

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**Poster session WED, 143**

Chronic relapsing inflammatory optic neuritis (CRION) in the neuroinflammatory clinic

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CRION is a rare cause of optic neuritis. It is usually bilateral, painful and associated with profound visual loss. Significant response to corticosteroid treatment is typical but relapse is common when treatment is withdrawn. We present 2 cases of possible CRION and discuss the diagnostic and management considerations.

Case 1: 50-year-old woman presented with right optic neuritis which spontaneously recovered. A year later she had left painful visual loss which improved with a short course of corticosteroids. MRI neuroaxis revealed left optic nerve enhancement. Non-specific, faint unmatched OCBs were detected. AQP4-IgG was negative. Nine months later she had further visual loss in her left eye. Prednisolone and azathioprine were commenced.

Case 2: 55-year-old woman with bilateral, painless visual acuity deterioration over two weeks. Investigations revealed negative anti-aquaporin 4 antibodies (AQP4-IgG), normal MRI of the neuroaxis, negative oligoclonal bands (OCBs) and visual evoked potentials showed bilateral delay. Serum ACE was slightly elevated. She was started on a tapering course of steroids and had significant visual acuity improvement.

The diagnosis of CRION involves the exclusion of other causes of optic neuritis, particularly multiple sclerosis (MS), Neuromyelitis Optica (NMO) and sarcoidosis. Correct diagnosis is important as aggressive and long-term immunosuppression is required.

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**Poster session WED, 145**

Human T-lymphotropic virus (HTLV)-associated encephalitis

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Clinical features of human T-lymphotropic virus type 1 (HTLV-1)-associated myelopathy (HAM) are predominantly consistent with cord pathology. Imaging and autopsy studies have also demonstrated brain inflammation in HAM though this is generally subclinical. Six cases (of whom four had HAM) have previously been reported with encephalopathy in HTLV-1 infected patients, without alternative identified aetiology. Histopathology was reported in three of these, with perivascular CD8+ lymphocytic infiltrates in the brain, similar to that seen in the spinal cord in HAM.

We describe three further cases of encephalitis in the UK HAM cohort (n=142). Clinical features included: reduced consciousness; fever/hypothermia; headache; seizures; focal neurology. Investigation showed: raised CSF protein; pleocytosis; raised CSF:peripheral blood mononuclear cell HTLV-1 proviral load ratio; MRI either normal or showing diffuse, partially reversible leucoencephalopathy. No alternative aetiology was found. Two died following 1–5 recurrent episodes over a period of 1–5 years, despite responses to immunosuppression.

We reviewed the existing literature together with our new cases. 7/9 had concurrent HAM. All seven deteriorated sub-acutely preceding encephalopathy. 7/9 were treated with IV steroids, six improved. Six died, five despite steroids.

We propose that HTLV-associated encephalopathy may be part of the spectrum of disease seen in HAM itself.

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Poster session WED, 148
Imaging findings in autoimmune encephalitis: a retrospective review

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Background: Neuroimaging findings in autoimmune encephalitis may include normal MRI as well as limbic and extra-limbic involvement. Prompt recognition allows early immunosuppression and improved outcomes.

Methods: Retrospective review of patients with Autoimmune encephalitis over the last 5 years.

Results: We identified N-methyl-D-aspartate receptor (NMDAR) n=8, voltage gated potassium channel (VGKC) n=11, and leucine-rich glioma inactivated 1 (LGI1) n=11 encephalitis patients. 1/8 NMDAR encephalitis patients had abnormal MRI findings of T2 hyper intense signal in right anterior temporal and bilateral frontal and left insular lobe. DWI sequence showed restricted diffusion. 4/11 with VGKC encephalitis had positive MRI findings. Two patients had limbic involvement while one also had involvement of basal ganglia. Two patients had modest cerebral atrophy. Four patients had normal MRI findings. MRI scan was not available for three patients. 5/11 LGI1 encephalitis patients had bilateral mesial temporal lobe changes. In one patient, MRI could not be done due to permanent pacemaker. Five patients had normal MRI findings.
Conclusions: In our series, 33% patients had abnormal MRI findings consistent with a diagnosis of autoimmune encephalitis, which is lower than reported in literature. High clinical suspicion should lead to prompt diagnosis even in the absence of typical encephalitic changes on MRI.

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**Poster session THUR, 149**

ANCA/MPO vasculitis presenting with bilateral ischaemic optic neuropathy

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An 80 year old gentleman presented with bilateral, sequential ischaemic optic neuropathy. He initially developed progressive loss of vision in left eye with loss of colour vision and subsequently developed similar symptoms in the right eye with headaches, weight loss, malaise and lethargy. His visual acuity dropped to 6/12 on the right and counting fingers on the left. He had a dense central scotoma in left eye with left-sided RAPD but no other focal neurological deficits.

Blood tests revealed an ESR of 107 with an MPO ANCA titre of 19. MRI brain with contrast showed prominent meningeal enhancement and infiltration with ischaemic changes in the brain. CSF analysis revealed WCC of 24 (95% lymphocytes), RCC 22 and protein 0.4g/L with negative bacterial culture. Temporal artery biopsy was normal.

He was treated initially with IV methylprednisolone and 6 cycles of IV cyclophosphamide and subsequently put on methotrexate. His systemic symptoms have resolved completely and his visual acuity continues to gradually improve.

MPO-ANCA vasculitis can mimic temporal arteritis and should be considered in patients presenting with an ischaemic optic neuropathy. It is also a treatable cause of meningeal disease.

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**Poster session THUR, 150**

Treatment and outcomes in primary angiitis of the CNS (PACNS)

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Background: PACNS is a rare and heterogeneous disorder with many uncertainties regarding management and outcomes. Published adult UK series total just 20 patients.

Method: Hospital record search of an adult tertiary neurosciences centre identified 14 cases of PACNS from 1033 potential cases over 20 years.

Results: All 14 cases were ‘definite’ by Calabrese Criteria (1988), confirmed by brain biopsy in 8/14 and by angiography in 6/14.

The median age of onset was 52 years and most presented with focal deficits (86%), headache (36%) and cognitive change (29%). MRI showed multifocal deep white matter change in 86% and infarcts in 50%. Gadolinium enhancement was seen in 43%. Two patients had solitary ring-enhancing lesions and one patient had signs of cord ischaemia. CSF was abnormal in 90%.

All patients received corticosteroids, 11/14 cyclophosphamide, 3/14 Mycophenolate Mofetil, 3/14 Methotrexate and 2/14 Azathioprine. At 13.3 months median follow-up, all but the two patients with solitary lesions remained on immunosuppression. Clinical relapses occurred in 30% and radiological relapse in one case despite immunosuppression.

Only 62% had a favorable outcome (mRS 0-2). One patient died as a direct consequence of PACNS and one patient died due to co-morbidities.

Conclusion: PACNS remains a treatable neuroinflammatory disease with poor outcomes.
**Poster session THUR, 153**

Antibodies against the voltage-gated potassium channel complex

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Voltage-gated potassium channel (VGKC) complex antibodies have been associated with a spectrum of presentations including peripheral nerve hyperexcitability (PNH), Morvan’s syndrome, autoimmune encephalopathy, epilepsy and recently psychosis.

We retrospectively reviewed the medical records of 70 patients from the Greater Manchester Neuroscience Centre, who had tested positive for VGKC-complex antibodies between 2012 and 2015 to identify the clinical relevance of positive results.

The majority were diagnosed with autoimmune encephalopathy(19) followed by epilepsy(14), psychosis(10) and PNH(6). The remaining fifteen had other neurological presentations and six had no primary neurological disorder. 39/70 patients who had antibody titres >400 pM, were diagnosed with autoimmune encephalopathy(19), epilepsy(9), psychosis(4), PNH(3) and other disorders(4). 24/39 patients, who received treatment with one or a combination of corticosteroids, intravenous immunoglobulins, cyclophosphamide, plasma exchange, azathioprine or rituximab, had a diagnosis of autoimmune encephalopathy(18), epilepsy(2), psychosis(2) and malignancy(2). 16/24 were treatment responsive. 3/31 patients with lower titres were also treated, but only one with the classic phenotype (PNH) responded to treatment.

The classic phenotype often had a titre >400pM. PNH may have a titre ≤400pM. The patients without classic presentations typically had titres ≤400pM. Consistent with previous studies, clinical phenotyping and antibody titre helped to determine the relevance of VGKC-complex antibodies.

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**Poster session THUR, 155**

Autonomic function testing in autoimmune autonomic ganglionopathies

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Introduction: Autoimmune autonomic ganglionopathies (AAG) are an increasingly diagnosed cause of autonomic failure. In 50% of patients, nicotinic ganglionic acetylcholine receptor (α3-AchR) antibodies are found. The presentation includes orthostatic hypotension, gastrointestinal and bladder dysfunction, abnormal pupillary responses and sicca symptoms. Physiological changes are documented with serial autonomic function testing. Gold standard therapy is not well established; however treatment with repeated plasma exchange appears to alter disease course.

We provide the first description of consecutive autonomic function tests of one patient with seronegative AAG versus one patient with seropositive AAG both treated with serial plasma exchanges.
Methods: We compare ten parameters – time tolerated in head up tilt (HUT), lowest tilt heart rate (HR), systolic and diastolic blood pressures (BP), HR Valsalva phase 2 and 4, Valsalva ratio, change in catecholamines, HR response to deep breathing and antibody titre.

Results: HUT time, Valsalva ratio and the lowest tilt diastolic BP correlate best with clinical course over time. The α3-AchR titre also correlates with clinical improvement in the seropositive AAG patient.

Conclusions: We propose that repeated HUT time, Valsalva ratio and lowest tilt diastolic BP should be recorded in patients with AAG to determine treatment response and to assist in deciding treatment continuation.

Poster session THUR, 156
Safe prescribing of immunosuppression: quality improvement project
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Background: The use of immunosuppression therapies in Neurology has extended exponentially since they were first used in the 1970s for myasthenia gravis. However there are no NICE or neurology specific guidelines in this area for Neurologists to refer to in their clinical practice.

Method and Results: This 2014 retrospective case notes audit compared medical documentation to ‘10 key statements’ pertaining to the safe use and monitoring of immunosuppression therapies. This is a framework for clinical practice that was first published by The British Association of Rheumatology and The British Association of Dermatology in 2008.

A number of key areas of poor documentation around drug safety, pregnancy and vaccinations were identified and in response generic and drug specific safety “check-lists” and guidelines were produced, to be filled out with all patients, prior to starting therapies.

In 2016 following the implementation of the quality improvement project, a repeat audit of patient’s medical notes showed a clear improvement in documentation.

Conclusions: Drug specific guidelines led to an improvement in documentation and we believe that this also reflects safer prescribing and improved clinical practice. We are now in the process of developing guidelines to be used throughout the entire Northern Deanery.

Poster session THUR, 158
Susac’s syndrome: treatment and outcomes in three cases
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Background: Susac’s syndrome (SS) is a rare, autoimmune microangiopathy causing a triad of branch retinal artery occlusions, sensorineural hearing loss and brain lesions. Published data on immunotherapy and outcomes is very limited.
Method: Single centre case note review. Electronic hospital records between 1996 and 2017 were searched. 277 possible cases were reviewed.

Results: 3 cases (2 female, 1 male) with the full SS triad were identified. Median age of disease onset was 35.2 years with headache (n=3), confusion (n=1), hearing loss (n=3), vertigo (n=2) and visual field loss (n=2). Time from onset to diagnosis with the full triad was 3-23 months. MRIs showed characteristic corpus callosum involvement. All patients received high-dose corticosteroids as acute therapy. Case 1 was treated with Mycophenolate Mofetil (MMF) and Prednisolone for 27 months, and followed up for a further 8 months. She remained relapse-free. Case 2 relapsed on steroid-reduction, so received Rituximab followed by MMF and Prednisolone. She has now been stable for 14 months. Case 3 was intolerant to high-dose corticosteroids, Cyclophoshamide and MMF. He relapsed off treatment then commenced Azathioprine. Duration on Azathioprine is 14 months with one further relapse.

Conclusion: SS is rare but causes significant morbidity. Recognition of characteristic findings and early immunotherapy improves outcomes.

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Poster session THUR, 159
Radiological findings in two patients with autoimmune GFAP astrocytopathy

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Background: Autoimmune Glial Fibrillary Acidic Protein (GFAP) Astrocytopathy is a relatively new category of immune-mediated disease involving the central nervous system that demonstrates a widely variable spectrum of clinical presentations, ranging from the relatively mild or subacute onset of cognitive impairment, seizures, encephalopathy, meningeal symptoms to more complex forms of encephalomyelitis.

Materials & Methods: We present a radiological review of two cases which were recently diagnosed in our institution. They presented with fever, meningoencephalitis and bilateral papilloedema. CSF antibody analysis (GFAPα-IgG) from Mayo Clinic confirmed the diagnosis of GFAP in both cases.

Results: The typical radiological findings in both of the cases were a radial pattern of enhancement in brain and longitudinally extensive myelitic lesions in the spinal cord. The first patient improved with immunosuppression treatment. The second patient had a significantly more severe clinical presentation with drug-refractory progression, who later died.

Conclusion: Patients presenting with subacute onset of cognitive impairment, meningoencephalomyelitis and papilloedema should raise the suspicion of autoimmune GFAP astrocytopathy. Though it is a relatively new disease entity, the radial pattern of enhancement and long spinal cord lesions on imaging are striking and CSF and serum antibodies are highly specific.

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Poster session WED, 162
Cognitive impairment in a Greek MS patient cohort using BICAMS
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Introduction

Cognitive impairment (CI) can present in 40-70% of MS patients and in the early stages of the disease. The Brief International Cognitive assessment for MS (BICAMS) is a brief, practical and potentially universal battery for cognitive assessment in MS.

Aim: To correlate cognitive function with clinical parameters as disease type, EDSS, and disease duration

Methods: The cognitive function was measured with the validated to the Greek population BICAMS tool, which consists of the Symbol Digit Modalities Test (SDMT), the Greek Verbal Learning Test (GVLT) and the Brief Visuospatial Memory Test-Revised (BVMT-R).

Results: 36% patients classified as impaired according to the BICAMS battery. Progressive types of disease had worst scores than the relapsing in the SDMT (MD=1.73; 95%CI: 0.46, 3.0; p=0.009), GVLT (MD=1.77; 95%CI: 0.82, 2.72; p=0.001) and BICAMS z-score (MD=1.39; 95%CI: 0.54, 2.24; p=0.002). The two groups were also different in EDSS (p<0.001). EDSS showed correlation with BICAMS test. Disease duration did not correlate with CI. Age was identified as a risk factor of CI.

Discussion: Early management of CI can lead to improvement in the patient’s quality of life. Progressing types of the disease might benefit from early cognitive assessment in the disease course.

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Poster session WED, 163

Monitoring for outcome assessment and trial recruitment of pwMS

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Background: The time constraint of NHS care is difficult to reconcile with the comprehensive neurological assessment required to complete a mandatory EDSS for NHS England funded disease modifying treatment of people with multiple sclerosis (pwMS). We report our experience with parametric data collection in order to (i) inform DMT decisions and (ii) improve characterisation for recruitment of pwMS in clinical trials.

Methods: We implemented a battery consisting of the symbol digit modality test, 9-hole-peg-test, 25ft walking test and ABILHAND. pwMS were encouraged to sign up to the MS Register to record patient reported outcomes and "webEDSS". Data from the MS Register and BartsMS Database were electronically linked.

Results: 334 pwMS at different disease stages (EDSS 0 - 8.5) have been assessed at least annually. Of these, 64% had a relapsing and 36% a progressive disease course. Clinically meaningful data was obtained and displayed in an engaging portal for interpretation by the clinical team and pwMS. Conclusion: It’s feasible to implement multidimensional monitoring of pwMS to benefit (i) management of pwMS and (ii) trial recruitment, particularly for pwMS with EDSS >6.5. Longitudinal follow-up and data analysis is
underway. Standardisation of a simple, regularly collected, dataset may improve performance assessment between centres.

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**Poster session WED, 164**

**EQ-5D in the assessment of relapse recovery in MS**

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Rationale: 50% of multiple sclerosis (MS) relapses result in permanent disability. Modelling recovery from relapse enables cost-effectiveness of interventions to be evaluated. The expanded disability status scale (EDSS) is cumbersome in clinical practice and may not reflect patient experience. The EQ-5D is a standardised measure of health status and a common currency used by agencies such as NICE.

Aim: To compare measurable recovery from relapse using EDSS and EQ-5D.

Method: EDSS and EQ-5D-3L were collected during clinician defined relapse and at 2-months follow-up, in 89 patients identified in a regional rapid access clinic.

Results: Median EDSS in relapse was 5.0 and 3.5 at follow-up; 67 (75%) patients experienced improvement in EDSS. The proportion of patients with EQ-5D scores of level 1 (fewest symptoms) increased in all 5 domains at 2 months, although anxiety/depression was the most resistant to improvement. Of those with EDSS improvement, only 49 (73%) reported improvement in their health state (EQ-5D).

Conclusion: EDSS improvement following relapse is not always accompanied by patient-reported improvement in health state (EQ-5D), which may be more effective in identifying ongoing health issues. Low-level discrepancies may also inform on the relative merit of EQ-5D versus EDSS in assessing recovery.

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**Poster session WED, 165**

**The management of cognitive and behavioural symptoms in MS**

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Background: Approximately half of MS patients (pwMS) experience cognitive impairments including domains such as memory, concentrations, executive functions, which can be exacerbated by mood disturbances and fatigue. NICE guidelines (CG168) recommend proactive identification of cognitive symptoms, assessment and referral to neuropsychology services or occupational therapy.

Aim: To assess the local departmental MS service with regards to diagnosis and management of cognitive and behavioural symptoms.

Method: We conducted a retrospective audit of pwMS attending the specialist MS clinic since March 2017. Records were reviewed for documented evidence of: a discussion about
cognitive and behavioural changes; use of assessment tools; management; referral. Data was also collected on demographics, presence of comorbidities, use of disease modifying therapy, and cognition-modulating medication.

Results: 69% of pwMS demonstrated cognitive or behavioural symptoms including: fatigue (71%), poor memory (28%), depression, sleep disturbance, and concentration difficulties. Almost half expressed multiple symptoms. 47% of patients were referred for further management with OT, psychology services, or counselling.

Conclusion: This study highlights the ongoing need for greater focus on identification of cognitive and behavioural symptoms in the MS population. Furthermore, simple assessment tools such as questionnaires should be considered within the clinic for monitoring cognitive symptoms and response to intervention.

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**Poster Session 167**

Socioeconomic status and progression of disability in MS

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There is evidence that socioeconomic status (SES) is associated with multiple sclerosis (MS) incidence; however it is less clear whether there is also an association with long-term prognosis.

3113 patients were selected from the MS registries of British Columbia, Canada (n=2069), and Cardiff, Wales (n=1044). SES, based on neighbourhood-level average income, was measured at onset of MS. Cox proportional hazards regression was used to analyse the association of SES with time to sustained and confirmed EDSS 6.0 and EDSS 4.0. The association between SES and EDSS scores was assessed longitudinally by a linear regression model fitted using generalised estimating equations (GEE) with an exchangeable working correlation structure. All models were adjusted for age at onset, sex, year of onset, initial course and DMT. The cohorts were analysed individually and results combined using meta-analysis.

SES was associated with hazard of reaching EDSS 6.0 (adjusted hazard ratio [aHR]=0.90, 95%CI 0.89 – 0.91), and 4.0 (aHR=0.93, 0.88 – 0.98). GEE modelling confirmed association of SES with EDSS (β=-0.13, [-0.18 -0.08], p<0.001). We found evidence that lower SES is associated with poorer outcomes. Reasons for this are complex but may include lifestyle or comorbidity. Our findings are relevant for planning and development of MS services.

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**Poster session WED, 168**
Blood-brain barrier imaging with dynamic contrast-enhanced MRI

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Background: Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) can detect subtle blood-brain barrier (BBB) permeability. We developed a protocol and conducted experiments to validate the technique.

Methods: 12 subjects with relapsing-remitting multiple sclerosis (RRMS) and 13 controls were recruited. Whole-brain 3D DCE-MRI at 3 Tesla was used to calculate the influx constant Ki (Patlak method). Values were derived for manual regions of interest (ROI) as well as segmented tissue masks. In controls, cerebral blood volume (CBV) was measured in grey and white matter.

Results: In RRMS, Ki in visibly-enhancing lesions was significantly higher than in normal-appearing white matter (NAWM) (p = 0.002). Ki in NAWM was significantly higher in RRMS than controls, by both ROI (p = 0.014) and segmentation (p = 0.019) methods. In controls, Ki was significantly higher in grey than white matter (p = 0.001). CBV (and therefore vascular surface area) was also significantly higher in grey matter (p = 0.005), with a mean ratio of 1.9.

Conclusions: Our method produces results in line with the expected behaviour of a BBB permeability marker, and the grey/white matter CBV ratio is in agreement with the histologically-established value.

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Poster session WED, 170

The utility of brain FDG-PET in a patient with natalizumab associated PML-IRIS

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Natalizumab, a highly effective disease modifying drug used in relapsing remitting multiple sclerosis (RRMS), is associated with progressive multifocal leukoencephalopathy (PML), a fatal intracerebral demyelinating disease caused by the JC virus that can be worsened with concurrent use of steroids. Stopping natalizumab in the context of PML can cause immune reconstitution inflammatory syndrome (IRIS) that can be treated with steroids. IRIS can be indistinguishable from PML on MRI - thus causing a clinical conundrum.

We describe a woman with RRMS on Natalizumab who developed dysarthria and right-sided hemiparesis. MRI demonstrated non-enhancing peridentate white matter signal abnormality in the right middle cerebellar peduncle (RMCP). Cerebrospinal fluid JC virus DNA was >1million copies/ml. PML was diagnosed and Natalizumab withdrawn. Four weeks later she developed bulbar weakness and left-sided hemiparesis despite falling JC virus DNA. Repeat MRI demonstrated new extensive pontine changes consistent with PML-IRIS.
FDG-PET imaging confirmed focal areas of hypometabolism at the original site of PML and multiple areas of hypermetabolism in the left pons and middle cerebellar peduncle, suggestive of IRIS. Her clinical deterioration was attributed to IRIS and Prednisolone was commenced. In this case FDG-PET scanning helped distinguish between PML and IRIS, guiding patient management.

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**Poster session THUR, 171**

Natalizumab effectiveness and safety in TOP UK patients

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Introduction: The TYSABRI® Observational Program (TOP) is an ongoing, global open-label study enrolling natalizumab-treated relapsing-remitting multiple sclerosis patients in real-world settings. Country-specific data can provide information on natalizumab’s benefit-risk in local clinical practice.

Methods: Clinical outcomes in UK and rest of world (ROW) TOP patients were compared.

Results: As of May 2016, 134 UK and 5793 ROW patients were enrolled in TOP. Mean baseline Expanded Disability Status Scale (EDSS) score was 4.27 in the UK and 3.45 in ROW. Mean years on natalizumab was 3.52 in the UK and 3.04 in ROW. Annualized relapse rate (ARR) decreased by 89.7% (from 2.21 pre-natalizumab to 0.23 post natalizumab initiation; P<0.0001) in the UK and by 89.0% (from 1.99 to 0.22; P<0.0001) in ROW. In both cohorts, ARR decrease by baseline EDSS score was 91.0%–93.2% for <3.0 and 87.3%–88.9% for ≥3.0; mean EDSS score change from baseline over 6 years was <1.0. Overall, 9 of 134 UK patients (6.7%) experienced ≥1 serious adverse event.

Conclusions: Natalizumab demonstrated similar effectiveness in the UK and ROW cohorts. Safety in the UK cohort was consistent with natalizumab’s established safety profile.

Support: Biogen

Disclosures: RN: grant/travel support from Biogen; KR, SL, SFSF, CS: Biogen employees.

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**Poster session THUR, 172**

CLARIFY-MS: Phase IV study of cladribine tablets and quality of life

Authors and disclaimer: 

Background: Relapsing multiple sclerosis (RMS) negatively affects health-related quality of life (HRQoL).

Objective: An open-label, single-arm, exploratory Phase IV study in centres in Europe and Australia will assess HRQoL in RMS patients receiving CT 3.5mg/kg (CT3.5).

Methods: Eligible patients will receive CT 3.5 (cumulative) over 2-years. HRQoL (Multiple Sclerosis Quality of Life-54 [MSQoL-54]) and other patient-reported outcomes (Fatigue
Severity Scale; Hospital Anxiety and Depression Scale; Treatment Satisfaction Questionnaire for Medication v1.4) will be assessed at baseline, and at 6, 12, 24 months.

Other outcomes include AEs, MRI measures (T1 Gd+ lesions, T2 lesions, brain atrophy), number of relapses, and disability/functioning measures (EDSS; 9-Hole Peg Test; Timed 25-Foot Walk and Brief International Cognitive Assessment for Multiple Sclerosis). The sample size estimation is based on the power to detect a mean difference of 5 points in MSQoL-54 composite score at 24 months vs. baseline.

Results: The study aims to recruit 356 adults with RMS by 2019. Final data are anticipated in 2022.

Conclusions: This study will explore the effects of CT on HRQoL outcomes, and describe the effects of CT on treatment satisfaction and disability/functioning.

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Poster session THUR, 173
LONGTERMS: 10-Year Experience of Fingolimod in RRMS Patients

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Objectives: Present results for up to 10 years of fingolimod treatment in RRMS patients.
Methods: LONGTERMS is an open-label, single-arm, extension study evaluating the long-term safety, tolerability and efficacy of fingolimod in patients who previously participated in earlier fingolimod studies. Key efficacy measures: annualised relapse rate (ARR), proportion of patients free of 6-month confirmed disability progression (6mCDP), annualised rate of new or newly enlarging T2 lesions (ARneT2), and annualised rate of brain atrophy (ARBA). Safety analyses: adverse events (AEs) and serious AEs (SAEs) frequencies.

Results: 3168 patients were included in the analysis. ARR decreased with longer exposure from 0.26 (Month [M] 0-12) to 0.20 (M0-60) and 0.19 (M0-120). Most patients remained free from 6mCDP at M60 (79.3%) and M120 (68.1%). ARneT2 decreased from 1.31 (M0-12) to 0.90 (M0-60), and 0.71 (M0-120). Change in brain volume was stable throughout the study (−0.37 [M12], −0.33 [M60] and −0.32 [M120]). Long-term exposure did not raise new safety concerns. No increase in frequencies of AEs or SAEs per year was observed over long-term fingolimod treatment.

Conclusions: Long-term follow-up confirmed the established safety profile of fingolimod. Treatment was associated with a sustained low level of disease activity as expressed by clinical and MRI outcomes.

Disclaimer: Previously presented at ECTRIMS 2017
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Poster session THUR, 174
The MAGNIFY-MS study: Mavenclad tablets in active RMS
Authors and Disclaimer:
Background: Cladribine tablets (CT) improve clinical and MRI outcomes in patients with active RMS, with significant differences versus placebo after 24 weeks.

Objective: Describe the design of a study to assess the onset of CT’s clinical and MRI effects in patients with active RMS.

Methods: MAGNIFY-MS is a 2-year prospective Phase IV trial (including approximately 100 centres in Europe). Eligible patients will receive two years treatment with CT 3.5 mg/kg cumulative dose. Frequent MRI assessments (including lesion count, lesion volume, brain volume and MTR) will be performed at screening, baseline and 1, 2, 3, 6, 12, 15, 18 and 24 months. Various T- and B-cell subtype counts and functional profiling (eg cytokine production) will be assessed. Clinical outcomes will include changes in cognition (SDMT), disability (EDSS/KFS, 9HPT, T25FW), relapses, NEDA, NEDAP and safety at timepoints up to 24 months.

Results: Aim: recruit 300 patients. Primary endpoint: change in the count of combined unique active lesions at end of 6 months versus baseline. Final outcomes expected in 2021.

Conclusions: MAGNIFY-MS will provide important information on the effects of CT, including early MRI changes, insights into effects on a range of disability and cognition markers, and detailed characterization of immune cell reconstitution.

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Poster session THUR, 177

Efficacy of alemtuzumab retreatment after 2 initial courses

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Efficacy of alemtuzumab retreatment (course [C] 3) after the initial 2 courses were evaluated (CARE-MS II, NCT00548405; extension, NCT00930553). Patients received alemtuzumab retreatment (12 mg/day, 3 consecutive days; ≥12 months apart) as needed for relapse and/or MRI activity or another disease-modifying therapy (DMT) per investigator’s discretion. Assessments 12 months before C3 and up to 3 years after C3: annualised relapse rate (ARR); improved/stable Expanded Disability Status Scale (EDSS) score (versus core study baseline); 6-month confirmed disability improvement (CDI). Patients receiving another DMT were excluded. Analyses included patients who received C3 or more, with data censored at the time of C4 if a fourth course was received. Through Year 6, 88% of patients entering the extension remained on study, with 45% receiving ≥1 retreatment. ARR decreased from 0.85 (12 months before C3) to 0.20 (12 months after C3; rate ratio [95% CI], 0.24 [0.17–0.34]; P<0.0001), and remained low (0.27) 3 years after C3. 68% of patients maintained stable/improved EDSS 12 months after C3. The percentage with CDI increased from 4% (12 months before C3) to 14% (12 months after
C3; P=0.0126). These findings demonstrate the efficacy of alemtuzumab C3 in patients with disease activity after the initial 2 courses.

Study support: Sanofi and Bayer HealthCare Pharmaceuticals.
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**Poster session THUR, 178**
Infections during grade 3/4 lymphopenia with cladribine tablets

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Background: In CLARITY, cladribine tablets 3.5 mg/kg (CT3.5) demonstrated efficacy in relapsing MS patients. The most common AE was lymphopenia, reflecting cladribine’s mode of action. Integrated safety analysis showed infection incidence was not higher in patients receiving CT3.5 vs. placebo, bar a small increase of herpes zoster (HZV).

Objective: Post-hoc analysis examined infectious AEs occurring concurrently with Grade 3/4 lymphopenia (G3/4) in CT3.5 treated patients.

Methods: The AE profile for CT3.5 during the periods of G3/4 was analysed. Adjusted-AE incidences per 100 patient years (Adj-AE/100PY) were calculated in a cohort of patients receiving CT3.5 monotherapy in clinical trials.

Results: Data are presented as Adj-AE/100PY: G3/4 vs. without G3/4. Adj-AE/100PY for any infections/infestations was 57.53 vs. 24.50. Infections were similar between periods. ≥50% cases with G3/4 were easily-treatable upper-respiratory-tract infections (nasopharyngitis:13.48 vs. 5.24; upper-respiratory-tract infection:9.67 vs. 3.41; pharyngitis:4.51 vs. 0.73). HZV occurred in 4 patients with G3/4 (4.50 vs. 0.73); cases were dermatomal and mild-to-moderate in severity. Single occurrences were reported for most infectious AEs. Opportunistic infections were single occurrences, not severe, serious or difficult-to-treat.

Conclusions: G3/4 increased frequency of infections but did not affect the type of infectious AEs in CT3.5 treated patients. HZV profile was uncomplicated, consistent with findings of previous analyses.

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**Poster session THUR, 179**
Ocrelizumab effect on NEDA in patient subgroups of OPERA I and OPERA II

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Background: In a pooled analysis of patients with relapsing multiple sclerosis in the Phase III OPERA I and OPERA II (NCT01247324/NCT014112333) studies, ocrelizumab increased the proportion of patients with no evidence of disease activity (NEDA) vs interferon β-1a (IFNβ1a); post hoc subgroup analyses are reported here.

Methods: NEDA (no 12-week confirmed disability progression, relapse, new/enlarging T2 lesions or T1 gadolinium enhancing lesions) rates were compared by Cochran–Mantel–Haenszel test on the pooled modified intent-to-treat (mITT) population (ocrelizumab, n=761 [600mg intravenously every 24 weeks]; IFNβ1a, n=759 [44μg subcutaneously three times weekly]; excludes patients with NEDA discontinuing for reasons unrelated to efficacy).

Results: Treatment benefit for NEDA in the mITT population with ocrelizumab vs IFNβ1a (47.7% vs 27.1%; p<0.001) was maintained across subgroups (ocrelizumab/IFNβ1a; p<0.001 unless stated): age (<40 years: 44.3%/22.6%; ≥40 years: 52.8%/33.7%), gender (male: 44.0%/22.2%; female: 49.7%/29.6%), prior [last 2 years] disease-modifying therapy (yes: 42.8%/23.9%; no: 49.5%/28.3%), prior relapses [last 12 months] (≤1: 49.2%/29.2%; ≥2: 44.2%/22.6%), baseline T1 Gd-enhancing lesions (none: 59.6%/38.8%; ≥1: 30.1%/10.2%) and baseline EDSS score (EDSS <2.5/<4.0: ocrelizumab 50.5%/50.3%, IFNβ1a 27.5%/26.4%; EDSS ≥2.5/≥4.0: ocrelizumab 46.0%/39.6%, IFNβ1a 26.9%/29.4% [NB: EDSS score ≥4: ocrelizumab/IFNβ1a p=0.043]).

Conclusions: Subgroup analyses were consistent with those of the overall pooled population on maintaining NEDA status.

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**Poster session THUR, 180**

Patient support program for RRMS patients treated with DMF

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Introduction: In the UK, the number of multiple sclerosis (MS) patients far exceeds the capacity of MS specialist nurses (MSSNs).

Methods: Biogen and IQVIA developed a remote, nurse-led, script-based telephone line providing educational assistance and supporting treatment adherence among relapsing-remitting MS (RRMS) adult patients receiving delayed-release dimethyl fumarate (DMF; TECFIDERA). Following DMF initiation, 8 calls are scheduled over the first 3 months,
followed by quarterly calls for the remainder of the first treatment year. The program began in March 2015; a new online treatment satisfaction survey started in July 2017.

Results: Based on summarized call data through November 2017, 941 total patients were enrolled from 136 UK hospitals, with a mean (median, range) of 6.9 (2, 1-117) patients/hospital. An average of 11.5 calls/patient were received. Across all 11 scheduled calls, the average time/call was 8.3 minutes. Over 33 months, cumulative DMF discontinuation among enrolled patients was 15.7%. Between July and November 2017, 31 patients on treatment for ≥1 year completed satisfaction surveys; 74% reported scores ≥4 (scale: 1 [poor] to 5 [excellent]).

Discussion: This program has been widely used and positively received across the UK by DMF-treated patients and may reduce the burden on MSSNs.

Support: Biogen. Disclosures on poster.

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**Poster session WED, 181**

Switching early from oral DMT to fingolimod in RRMS patients

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Objectives: Compare the effect of fingolimod in RRMS patients who switched from first-line oral disease modifying therapies (oDMTs) vs patients who switched from injectable disease-modifying therapies (iDMTs) in PASSAGE and PANGAEA 2.0 studies.

Methods: Patients who switched to fingolimod from dimethyl fumarate or teriflunomide (oDMT cohort; PASSAGE N=157, PANGAEA 2.0 N=72), or treatment naïve or after iDMTs (iDMT cohort; PASSAGE N=3484, PANGAEA 2.0 N=270). Annualised relapse rate (ARR) was recorded at months (M) 12 and 24.

Results: PASSAGE: Fingolimod reduced ARR at M12 to 0.30 and 0.26 (oDMT and iDMT cohort). Increasingly higher BL ARR were observed in the oDMT cohort patients who had received two or three DMTs (ARR=1.47 and 1.53).

PANGAEA 2.0: Fingolimod reduced ARR at M12 in both cohorts but was higher in the oDMT than in the iDMT cohort (0.19 vs 0.10, p=0.01). The BL ARR in the oDMT cohort increased with the number of failed DMTs before the switch (two DMTs, 1.58; three DMTs, 1.86) and was reduced with fingolimod treatment at M12 (two DMTs, 0.18; three DMTs, 0.21).

Conclusions: Fingolimod is effective in controlling disease activity in RRMS patients switching from other oDMTs. Switching early results in better relapse control within 1 year of initiation.


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**Poster session WED, 182**

Cladribine tablets effects on lymphocytes in MS patients
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Background: Lymphopenia is expected from the mechanism of action of cladribine tablets 3.5mg/kg (CT3.5)

Objective: Investigate absolute lymphocyte counts (ALC; 312 weeks) and subsets (240 weeks) in RRMS patients receiving 2 annual courses of CT3.5.

Methods: Pooled data from patients randomised to CT3.5 over 2 years in CLARITY/CLARITY-Extension inclusive of the PREMIERE registry (N=685).

Results: Baseline: median ALC=1.86×10⁹/L. Year-1: ALC reached nadir at 9-weeks post-treatment with CT3.5 (1.00×10⁹/L). Year-2: ALC reached nadir at Week-55 (0.81×10⁹/L), then recovered to the normal range (≥1.00×10⁹/L; Week-96). ALC was in normal range in 75% of patients by Week-144. Baseline median CD4+ were 851cells/μL. Nadirs occurred at Week-16 (385cells/μL) in Year-1 and at Week-60 (292cells/μL) in Year-2; values increased after nadirs and regained threshold (350 cells/μL, ~Week-120). Baseline median CD8+ were 378cells/μL. Nadirs occurred at Week-16 (239cells/μL; Year 1) and Week-72 (232cells/μL; Year 2). CD8+ recovered quickly after treatment and remained above 200cells/μL at all times. Baseline median CD19+ were 205cells/μL. Nadirs occurred at Week-9 (18cells/μL; Year-1) and Week-52 (31cells/μL; Year-2). CD19+ then reached threshold of 100cells/μL by the end of Year-2.

Conclusion: Lymphocyte recovery begins soon after CT3.5. ALC, CD19+ B and CD4+ T cells; reached threshold by 7.5, 12 and 18 months. CD8+ cells remained above threshold.


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Poster session WED, 183
Cladribine tablets effects on T Cell subsets in patients with early MS

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Background: Because of the durable clinical effects of cladribine tablets 3.5mg/kg (CT3.5) in patients with multiple sclerosis, the influence of treatment on cells with regulatory immune function is of interest.

Objective: Examine effects on central memory; effector memory; and naturally occurring regulatory (nTregs) CD4+ T cells after first administration of CT3.5 in ORACLE-MS.
Methods: Peripheral blood T-lymphocytes were immunophenotyped at baseline, and Weeks 5, 13, 24, 48 in CT3.5 treated patients (n=41). Absolute numbers and proportions of central memory (CD4+RO+CCR7+), effector memory (CD4+RO+CCR7-), Th1-type (CD4+CXCR3+), nTregs (CD4+CD25+CD127-), including naïve-like and memory-like nTregs were measured.

Results: Greatest median reductions in absolute numbers occurred at Week-13 for effector memory cells (-54%); Week-24 for central memory (-63%) and Th1-type cells (-51%); with similar/slightly increased levels at Week-48. There was ~5% reduction in proportion of central memory cells, but no change in proportions of effector memory and Th1-type cells. Absolute numbers of nTregs (-48%), naïve-like (-67%) and memory-like nTregs (-42%) decreased by Week-48. nTregs and naïve-like nTregs proportions were unchanged. Proportions of memory-like nTregs slightly increased up to 48-Weeks.

Conclusion: CT3.5 administration has a comparable effect on CD4+ T-cell subpopulations, with no dramatic shifts in proportions.

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**Poster session WED, 184**

Cladribine tablets in CLARITY patients with high disease activity MS

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Background: Patients with high disease activity (HDA) relapsing-remitting MS are less likely to attain no evidence of disease activity (NEDA; no relapses, MRI activity or progression).

Objective: Post-hoc analysis to compare the proportion of patients with NEDA with cladribine tablets 3.5 mg/kg (CT3.5) vs. placebo.

Methods: Patients from CLARITY were retrospectively stratified using 2 definitions of HDA based on relapse history, prior treatment, and MRI characteristics: HRA (n=261) and HRA plus disease activity on treatment (HRA+DAT) [n=289]). Data for patients treated with CT3.5 or placebo who fulfilled these criteria and achieved NEDA status were compared over the 2-years using odds ratios (OR) and 95%CI.

Results: HRA subgroup: 76% of CT3.5-treated patients were relapse-free and 84% were T1 Gd+ lesion-free vs. 49% and 31%, respectively, for placebo. HRA+DAT subgroup: 77% of CT3.5-treated were relapse-free and 85% were T1 Gd+ lesion-free vs. 50% and 32%, respectively, for placebo. In the HRA and HRA+DAT subgroups, 43.2% and 43.7%, respectively, of CT3.5-treated patients were disease activity free compared with 8.7%,
(OR:8.02;95%CI:3.93-16.35;p<0.0001) and 9.0% (OR:7.82;95%CI:4.03-15.19;p<0.0001) respectively, for placebo. In the overall population, composite NEDA score favored CT over placebo (OR:4.46;95%CI:3.18-6.26;p<0.0001).

Conclusions: Treatment with CT3.5 significantly increased the proportion of HDA patients with NEDA vs. placebo.

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Poster session WED, 185

CLARITY: MRI outcomes in high disease activity relapsing MS

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Background: The CLARITY study demonstrated the benefit of cladribine tablets 3.5 mg/kg (CT3.5) for patients with relapsing MS (RMS). Patients with high disease activity (HDA) RMS are at risk of clinical activity and disability progression.

Objective: Post-hoc analysis of MRI outcomes in CLARITY for CT3.5 vs. placebo.

Methods: Retrospective analysis using HDA definitions based on relapse history, prior treatment, and MRI characteristics: high relapse activity (HRA) and HRA plus disease activity on treatment (HRA+DAT).

Results: For cumulative new T1 Gd+ lesions, relative risk ratios (RRR) for both subgroups (HRA:0.087;95%CI:0.052-0.144;p<0.0001) (HRA+DAT:0.077;95%CI:0.046-0.128;p<0.0001) were lower for CT3.5 vs. placebo. Risk reductions (RR) (91% and 92%, respectively) were similar to the 90% reduction in the overall CLARITY population (0.097;95%CI:0.070-0.134;p<0.0001). Cumulative active T2 lesions RRR favoured CT3.5 vs. placebo for both subgroups (HRA:0.263;95%CI:0.180:0.383; p<0.0001) (HRA+DAT:0.254;95%CI:0.178-0.363;p<0.0001): RRs of 74% and 75%, reflecting the 73% overall population reduction (0.272;95%CI:0.221-0.335;p<0.0001). Cumulative combined unique lesions RRR favoured CT3.5 vs. placebo for HRA (0.212;95%CI:0.145-0.311;p<0.0001) and HRA+DAT (0.203;95%CI:0.141-0.291;p<0.0001): RRs were 79% and 80%, reflecting the 77% overall population reduction (0.234;95%CI:0.190-0.290;p<0.0001). There were no significant interactions between HDA and non-HDA subgroups.

Conclusions: The treatment benefit of CT3.5 on MRI outcomes was similar in HDA RMS subgroups and the overall CLARITY study population.

Disclaimer: [link]
Effect of cladribine tablets on immune cells in patients with MS

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Background: Cladribine tablets 3.5mg/kg (CT3.5) demonstrated efficacy in patients with early (ORACLE-MS) and relapsing MS (CLARITY/CLARITY-Extension).

Objective: Evaluate B, T lymphocyte and natural killer (NK) cell profiles after CT administration in ORACLE-MS, CLARITY and CLARITY-Extension.

Methods: Longitudinal evaluation of peripheral blood lymphocytes was conducted for patients receiving the CT (either part of the initial 3.5mg/kg active treatment groups or placebo switched to active treatment). Absolute lymphocyte counts (ALC) and subtype dispositions were evaluated at baseline, and Weeks 5, 13, 24, 48.

Results: Baseline distributions of ALC and temporal profiles of CD19+ B and CD4+ and CD8+ T lymphocytes were generally consistent across studies. Rapid reductions were observed for CD19+ B cells (~75% reduction; Week 5), with nadirs at Week 13 (~80% reduction). Reconstitution of CD19+ B cells towards baseline occurred from Week 24-48. Lesser, discontinuous reductions also occurred for CD4+ and CD8+ T cells that had not fully returned to baseline by Week 48. CD16+/CD56+ NK cells were transiently reduced with CT, with recovery evident at Weeks 24 (29%) and 48 (23%).

Conclusions: CT3.5 achieved early, discontinuous reduction of peripheral blood B cells, with rapid reconstitution towards baseline; a moderate, discontinuous reduction of T cells; and early, transient NK cell reductions.


Infections in ocrelizumab recipients from phase III studies

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Background: Ocrelizumab Phase III study safety findings in relapsing (OPERA I/II [NCT01247324/NCT01412333]) and primary progressive multiple sclerosis (ORATORIO [NCT01194570]) were reported; infections and serious infections are reported here. Methods: Ocrelizumab patients received 600mg intravenously every 24 weeks for 96 weeks (OPERA I/II) or ≥120 weeks (ORATORIO; 2×300mg infusions 14 days apart every 24 weeks). Controls received interferon beta-1a 44μg thrice weekly (IFNβ-1a; OPERA I/II) or placebo (ORATORIO). Infections were classified by MedDRA system organ class/preferred term.

Results: Non-serious infection rates in ocrelizumab-treated patients in OPERA were 58.4% (pooled analysis) and ORATORIO 69.8%; comparators were IFNβ-1a 52.4% and placebo 67.8%. Most infections were mild-to-moderate. Common infections (≥10% in either group) reported more in ocrelizumab treated patients were upper respiratory tract infections and either nasopharyngitis (OPERA) or influenza (ORATORIO); <1% of ocrelizumab-treated patients withdrew due to non-serious infections. Serious infections occurred in 1.3% (OPERA) and 6.2% (ORATORIO) of ocrelizumab-treated patients; comparators were IFNβ-1a 2.9% and placebo 5.9%. No infection-related deaths occurred in ocrelizumab treated patients in OPERA; two deaths occurred in ORATORIO (aspiration pneumonia and pneumonia [unrelated per investigator, related per sponsor]). No opportunistic infections were reported. Conclusion: Serious infection rates with ocrelizumab were numerically lower than with IFNβ-1a and similar compared with placebo.

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Poster session WED, 188

PANGAEA 2.0 interim results: switching to fingolimod

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Objectives: Present first interim results of PANGAEA 2.0 including effectiveness data of patients switching from other oral disease modifying therapies (oDMTs; dimethyl fumarate and teriflunomide) to fingolimod.

Methods: PANGAEA 2.0 is an ongoing non-interventional study. As of January 2017 PANGAEA 2.0 included 1419 patients, 1116 were included in this analysis of which 183 switched from other oDMTs to fingolimod.

Results: Slight differences were observed in the number of relapses 12 months (M) before baseline (mean ± SD) (1.4 ± 1.0 vs 1.6 ±1.0), the EDSS (2.2 ± 1.6 vs 2.4 ±1.7) and the MSSS (3.5 ± 2.5 vs 3.8 ± 2.5). 67.4% of the patients switched from dimethyl fumarate to fingolimod and 32.6% from teriflunomide. For 30.2% of the patients fingolimod was the second therapy since diagnosis. The annualized relapse rate (ARR, ±95%CI) 6M after switch to fingolimod was reduced from 1.6±0.22 to 0.2±0.05 for the patients switching from other oDMTs. For all patients the ARR was reduced from 1.3±0.06 to 0.14±0.02. The EDSS (± 95%CI) remained stable at 2.4±0.37 (2.5±0.50 respectively).

Conclusions: These data indicate that active disease patients switching from dimethyl fumarate or teriflunomide to fingolimod can benefit from this switch.

Disclaimer: previously presented at ECTRIMS 2017.

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**Poster session WED, 190**

Teriflunomide pregnancy registry: design and enrolment

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Introduction: Teriflunomide is contraindicated in pregnancy, based on developmental toxicity in rats and rabbits. During clinical development, despite requirements for contraceptive use, some pregnancies occurred. There were no signs of structural or functional deficits in newborns.

Methods: The multinational, prospective, observational International Teriflunomide Pregnancy Exposure Registry is enrolling teriflunomide-exposed pregnant women with MS. Signed informed consent is obtained prior to enrolment. In the UK, healthcare professionals submit information to the National Coordinating Centre (Manchester, UK). Infants are followed until 1 year old. Pregnancy outcomes, including birth defects and infant characteristics, are collected. Target recruitment: 196 women to achieve 104 live births, providing 80% power to detect 3.95-fold increase in risk of birth defects associated with teriflunomide exposure vs the European Surveillance of Congenital Anomalies (EUROCAT) network.

Results: As of 26/04/2017, 14 patients have been recruited from 7 European countries (none in the UK). Six healthy babies have been born to date. One patient had an elective termination not motivated by abnormal prenatal test results or concerns regarding potential birth defects.

Conclusion: This registry aims to provide data on pregnancy outcomes and infant development from teriflunomide-exposed women, which may help physicians provide better patient advice.

Study supported by Sanofi

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**Poster session THUR, 192**

Yearly lymphopenia rates in cladribine tablets-treated RMS patients

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Background: Cladribine tablets 3.5mg/kg (CT3.5) demonstrated efficacy in RMS patients in CLARITY/CLARITY-Extension. Lymphopenia was common (CT3.5: mechanism of action).

Objective: Evaluate whether lymphopenia persists following treatment/re-treatment with CT3.5 in CLARITY/CLARITY-Extension.

Methods: Lymphopenia by grade for patients randomised to CT3.5 throughout CLARITY/CLARITY-Extension (7mg/kg cumulative 4-year dose;N=186) are reported. Patients with Grade 0 (G0) lymphopenia (≥1.0×10^9 cells/L) before the first course of CT and G0/1 (≥0.8×10^9 cells/L) before subsequent treatment in Years 2 (Y2), 3 and 4 were analysed.

Results: 176 patients were G0 at the start of CLARITY (167 were G0/1; CLARITY-Extension). G3 lymphopenia was observed in 1% patients (Week-13, Y1), and in 7%, 11% and 12% patients at Week-12 in Y2, 3 and 4. In each year, G3 lymphopenia was observed in 1%, 4%, 4% and 4% patients (Week-24), in 1%, 2%, 2% and 2% patients (Week-36), and in 1% patients (Week-48) in Y2 only. G3 lymphopenia was reported in <18% patients at any time-point. No patients had G4 lymphopenia at the end of each treatment year.

Conclusions: In patients meeting treatment/re-treatment guidelines, no G4 lymphopenia occurred at the end of any treatment year; G3 lymphopenia was uncommon. Lymphocyte-based re-treatment criteria minimised the incidence of severe, sustained lymphopenia during 4-years’ treatment with CT.

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Poster session THUR, 194

Autologous haematopoietic stem cell transplant in MS

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Introduction: Autologous haematopoietic stem cell transplantation (AHSCT) is a very effective treatment in patients with highly active relapsing remitting multiple sclerosis (RRMS) who failed standard disease modifying therapies (DMTs).

Methods: We retrospectively reviewed the medical records of all patients with RRMS who received AHSCT in Sheffield.

Results: 25 patients with RRMS received AHSCT between July 2013 and July 2017. Their median age at diagnosis was 40 (22–56) years. All had highly active disease with gadolinium enhancing lesions on their pre-transplant MRIs. Eighteen patients had previously been treated with various DMTs and seven were treatment naïve. Median pre-AHSCT EDSS was 5.5 (2.5–7.5). Median follow up was 12 (3–42) months. Median post-AHSCT EDSS at the last follow up was 3 (1–6.5), p<0.001. No patient experienced further relapses following transplantation. Three patients had new lesions on their first follow up MRI at 6 months, but none had any new or enhancing lesions on subsequent MRI scans. Only routine transplant related toxicities were observed. One female and the wife of a male patient successfully conceived following AHSCT.

Conclusion: AHSCT is safe and effective in inducing remission in patients with highly active RRMS. Further studies are required to compare its efficacy with standard DMTs.

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Pregnancy outcomes in alemtuzumab-treated RRMS patients

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Murine studies show no alemtuzumab-related teratogenicity, but no controlled human clinical studies of alemtuzumab in pregnancy exist. In phase 2 (CAMMS223 [NCT00050778]) and phase 3 (CARE-MS I [NCT00530348], CARE-MS II [NCT00548405]) studies, patients received 2 annual alemtuzumab courses. Two extension studies provided longer-term evaluation (NCT00930553; TOPAZ [NCT02255656]). Pregnant/lactating patients were ineligible for further treatment but were followed up for safety. As of 1 April 2017, 248 pregnancies occurred in 156/972 alemtuzumab-treated female patients (mean [SD] age at conception, 32.5 [4.4] years; mean [SD] time from last alemtuzumab dose to conception, 33.5 [22.6] months; 16 within 4 months of dosing), with 218 completed, 14 ongoing, and 16 with unknown outcomes. Of completed pregnancies with known outcomes, 147 (67%) were live births with no congenital abnormalities or birth defects. There were 48 (22%) spontaneous abortions, 22 (10%) elective abortions, and 1 (0.5%) stillbirth. To date, there has been no signal for teratogenicity. Incidence of spontaneous abortions was comparable with treatment-naive MS patients (5%–21%) and the general population (17%–22%). Real-world data are currently collected by the International Lemtrada Pregnancy Exposure Registry, a prospective, non-interventional, observational safety study enrolling patients in ≥19 countries who become pregnant within 4 months of alemtuzumab exposure.

STUDY SUPPORT: Sanofi.
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Safe monitoring of natalizumab therapy in multiple sclerosis


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Natalizumab is one of the most effective therapies for relapsing-remitting Multiple Sclerosis. One complication is Progressive Multifocal Leucoencephalopathy (PML), a viral brain infection in patients already infected with JC virus. Monitoring of neurological symptoms, JC virus serology and regular brain imaging are required to ensure safe use of this therapy. Local audit data from 2015 indicated poor compliance with safety monitoring, with less than 25% of patients undergoing required investigations within the recommended time intervals. Subsequently a protocol was implemented to improve monitoring, with specialist nurses coordinating the requests for MRI scans and arranging JC virus serology, the frequency of which was determined according to the JC virus index.
The records of all patients receiving Natalizumab at the centre were audited to assess the impact of this protocol (n=155). 99.2% of patients were appropriately tested for JC virus and 95.3% were imaged within the recommended interval. Additional work with the informatics and virology team ensured serology results became more easily accessible. The use of a standardised nurse-led operating procedure has resulted in marked improvement in the safety monitoring of Natalizumab.

Poster session THUR, 199
MS DMT monitoring according to ABN guidelines & product specification
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Aim: Retrospective audit monitoring Multiple Sclerosis (MS) patients on Disease Modifying Therapies (DMT’s) according to Association of British Neurologists (ABN) guidelines (2015) and product specifications. This requires blood tests prior and during treatment and reviews by MS professionals.

Methods: MS nurse database identified patients, records were reviewed and data extracted including bloods, JC virus (JCV) testing, imaging, specialist tests and counselling. Analysis was presented to the MS team. Protocols and referral pathways were designed, and new patients were re-audited.

Results: The first cycle comprised of 280 patients, representing 325 individual DMT regimens. Prior to commencing treatments 90.7% blood tests, 58% imaging, and 60% JCV testing was completed on average. At 12 months, this decreased to 88.7% bloods, 30% imaging, and 25% JCV testing. Electronic records revealed that counselling documentation was sometimes incomplete. The second cycle analysed 55 patients showing improvement in Progressive multifocal leukoencephalopathy counselling and annual imaging.

Conclusion: Monitoring of bloods is done at a high standard, imaging and JCV testing less frequently meet monitoring guidelines. Factors influencing this include rural locations, variation in practice, and changing guidelines. Further work will include yearly follow-up, documentation of stopping criteria and regular review of monitoring guidelines. Patient involvement should be considered.

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Poster session WED, 201
A novel KIF1A mutation causing a neurodevelopmental disorder
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The KIF1A gene encodes a protein in the kinesin-3 family which drives movement along microtubules and is important for transport of synaptic vesicles. Biallelic mutations have been identified in autosomal recessive hereditary spastic paraplegia (HSP30) and hereditary sensory and autonomic neuropathy type 1A. More recently dominant
heterozygous mutations have been found in people with a more severe phenotype that includes developmental delay, spastic paraplegia, neuropathy, optic nerve hypoplasia and progressive cerebellar hypoplasia.

We report a female, now 22 years old, who has severe developmental delay, septo-optic dysplasia (requiring growth hormone and hydrocortisone replacement), sensorimotor axonal neuropathy, optic atrophy (now registered blind), non-progressive cerebellar hypoplasia, periodic limb movements and upper limb spasticity. She is extremely sensitive to gabapentin. A de novo \textit{KIF1A} variant, c.814A>G, was identified. This is a novel missense variant (p.N272D) in the kinesin-motor domain.

This case shows a phenotype consistent with previously described heterozygous \textit{KIF1A} mutations and we believe represents a unifying diagnosis for her neurological disabilities. No previous cases describe non-progressive cerebellar hypoplasia nor septo-optic dysplasia requiring pituitary hormone replacement. This novel mutation therefore expands the phenotype associated with \textit{KIF1A} mutations. We hypothesize that her sensitivity to gabapentin may be due to the \textit{KIF1A} mutation.

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\textbf{Poster session WED, 202}

\textbf{Lamb-Shaffer syndrome: Importance of SNP array in diagnosing neurodevelopmental syndromes}

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We describe the seizure phenotype of a 26 year old lady who presented with a probable photic-induced convulsion on a background of mild intellectual disability, facial dysmorphia, fused cervical vertebrae and ventricular septal defect. There was no prior history of seizures.

Routine EEG was polyrhythmic with a prominent photoparoxysmal response at 14Hz and 40Hz. CT head was normal. A SNP array demonstrated a rare 51kb deletion at 12p12.1 which disrupts the \textit{SOX5} gene.

\textit{SOX5} is a developmentally important gene encoding a transcription factor that plays a role in multiple developmental pathways including of the nervous system. Loss of function of this gene is associated with Lamb-Shaffer syndrome, first characterised in 2012 with global developmental delay, intellectual disability, mild dysmorphic facies, language impairment and variable skeletal abnormalities.

3 of the original cohort of 16 patients described experienced seizures and the nature of their epilepsy was not further defined. Only a further 7 cases have been reported to date, none of whom experienced seizures. Our case helps to broaden the phenotype of Lamb-Shaffer syndrome, highlights the importance of looking for copy number variation and poses questions regarding the neurobiology of photo-sensitivity.

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**Poster session WED, 203**

Vanishing white matter disease due to variant mutations in the EIF2B-1 gene

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This otherwise fit and well 25 year old gentleman presented with new onset intermittent stabbing headaches associated with generalised tiredness and one nocturnal seizure. His neurological examination was normal and there were no dysmorphic features. He continues to remain intact neurologically.

Initial CT Brain showed periventricular low attenuation changes bilaterally associated with bi-frontal atrophy. MRI Brain confirmed extensive periventricular White Matter T2 high signal changes in keeping with Leukomalacia and generalised cerebral atrophy.

Genetic testing revealed 2 variant mutations in the EIF2B1 gene, of which one has been previously reported pathogenic and the other is a frame shift variant – likely pathogenic consistent with a diagnosis of vanishing White Matter Leukodystrophy.

VWM leukodystrophy is an autosomal recessive disorder characterized by variable neurologic features, including progressive cerebellar ataxia, spasticity, and cognitive impairment associated with WM lesions on brain imaging. The prevalence is unknown; and age at onset can range from early infancy to adulthood. Rapid neurological deterioration can occur following minor head trauma, infections and stress. Mutations in EIF2B1, EIF2B2, EIF2B3, EIF2B4 and EIF2B5 genes cause leukoencephalopathy with Vanishing White Matter.

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**Poster session WED, 209**

A case report of hyperhomocystinemia due to homozygous MTHFR mutation

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Homocysteine is metabolized via two pathways, remethylation or trans-sulfuration. The former requires 5-methyltetrahydrofolate reductase (MTHFR) and Vitamin B12, the later requires cystathione-beta-synthetase and Vitamin B6. Mutations in the MTHFR genes affect the enzyme activity to various degree and manifestations can be neuropsychiatric, vascular & neurodegenerative. Here we report a case of severe homocysteinemia secondary to two homozygous MTHFR gene mutations.

32 year old pregnant female initially presented in 2014 with grand mal seizure. After being seizure free on antiepileptics, she was admitted again to hospital in January 2017 with headaches, confusion, slurred speech and neuropathic pain in feet. She developed spastic paraparesis and her condition remained critical for several weeks due to refractory seizures and low GCS.

She was on warfarin for recurrent DVTs and had family history of mental health problems. Homocysteinemia was discovered when he was screened for metabolic causes and
leucodystrophies. MRI of the brain showed cerebral, cerebellar and brain stem atrophy. Neurophysiological studies were normal. Genetic testing found her to be homozygous for 2 MTHFR mutations. She was commenced on calcium folinate and parenteral B12, to which she responded really well.

Thorough history, targeted investigations and systematic approach are keys for diagnosis of rare metabolic disorders.

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**Poster session THUR, 213**
An unusual case of cluster acetylcholine receptor antibody positive myasthenia gravis

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A 73-year-old builder presented with fatigable ptosis and ophthalmoplegia. He was started on pyridostigmine for presumed ocular myasthenia gravis (MG). Despite making an initial improvement he subsequently developed dysarthria, dysphonia and a head drop within 3 weeks. At this time, he also had mild proximal weakness and marked asymmetrical distal weakness of the upper limbs and mild distal lower limb weakness.

Conventional serological screening for acetylcholine receptor (AChR) and muscle specific kinase antibodies were negative. However, extended testing using a cell-based cluster assays demonstrated AChR antibody positivity. Repetitive nerve stimulation demonstrated significant decrement more prominent in distal muscles.

Despite high dose prednisolone, azathioprine, several courses of IV Immunoglobulins and plasma exchange the patient has had frequent admissions to the high dependency and intensive care setting with respiratory failure.

Cluster AChR antibody positive MG has been described only within the last decade and is usually mild and treatment responsive. This is the first case reported to have required intubation and ventilation due to respiratory failure. This case highlights the importance of extending the routine panels for antibody testing in patients with “seronegative” MG and the need to remain vigilant in patients with cluster-AChR positive disease.

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**Poster session THUR, 215**
Lessons in the diagnosis and management of POEMS syndrome

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We present the case of a 46-year old man who developed a rapidly progressive sensorimotor neuropathy and skin changes. He was diagnosed with Guillain-Barré Syndrome, and subsequently CIDP, but his condition continued to progress despite IVIG treatment and plasma exchange. On transfer to the National Hospital of Neurology and Neurosurgery, six months after the onset of illness, he had profound lower limb weakness with power 0 distal to his knees, and upper limb involvement to the elbows. Deep tendon
reflexes were absent, and vibration and joint position sense were reduced peripherally. Nerve conduction studies identified a length-dependent demyelinating polyneuropathy with secondary axonal loss, and blood tests demonstrated thrombocytosis, endocrine dysfunction, and a raised VEGF. Two FGD-avid mixed sclerotic and lytic bone lesions were identified on PET-CT. Biopsy of these lesions demonstrated plasmacytomas with lambda light-chain restriction, and bone marrow biopsy revealed 4% plasma cells, with polytypic light chain staining. A diagnosis of POEMS syndrome was made, and he was initiated on lenalidomide and dexamethasone treatment. With reference to this case we will discuss the challenges in the diagnosis of POEMS syndrome. Additionally, we will outline the therapeutic options available; providing an algorithm to simplify the treatment selection process.

Poster session THUR, 216
Myasthenia gravis, thymoma and Good’s syndrome

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Myasthenia gravis (MG) is in 15% of cases a paraneoplastic phenomenon secondary to a thymoma. A subset of these will have both a thymoma and associated immunodeficiency known as Good’s syndrome. Immunological features include hypogammaglobulinaemia, a reduction in peripheral B cells, CD4+ lymphopenia, and reversal of CD4/CD8 ratio.

We present two cases followed by a literature review:
1. 52 year-old man presented with dysphagia, diagnosed as MG. He was found to have a stage 4a thymoma (histology B2), subsequently resected. He was noted to have a reduction in peripheral B cells and CD4+ lymphopenia suggestive of Good’s syndrome. He has also had chronic diarrhoea and recurrent pulmonary infections with Pseudomonas, Klebsiella and Mycobacterium abscessus. Current immunotherapy includes prednisolone.
2. 42 year-old woman presented with a myasthenic crisis requiring ITU admission. She was found to have a thymoma (histology B3), treated with resection and adjuvant radiotherapy. Peripheral B cell reduction led to a diagnosis of Good’s syndrome. She is currently in remission on prednisolone, mycophenolate mofetil and 6-weekly immunoglobulin infusions.

These cases illustrate that Good’s syndrome is an important differential when managing patients with myasthenia gravis, especially as the immunodeficiency may precede or occur after the diagnosis of a thymoma.

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Poster session THUR, 217
Salmonella gives you wings

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A 35-year-old British man based in Pakistan presented with a febrile illness, associated with hepatosplenomegaly. Salmonella paratyphi A was isolated from blood cultures and he
was treated with oral and intravenous cephalosporins. 3 weeks later, he developed polyarthralgia and right scapular winging. 5 weeks after the initial episode, fevers recurred with new right upper limb neuropathic pain. Examination showed weakness of right serratus anterior, deltoid and triceps, and reduced sensation in left lateral cutaneous nerve of forearm (LCNF) distribution. Neurophysiology showed abnormal sensory responses in the left LCNF and right superficial peroneal nerve, and abnormal EMG in right serratus anterior and right pronator teres. MRI brachial plexus showed no abnormal enhancement in the plexus. CSF was normal. *Salmonella paratyphi A* was again cultured from blood and he was re-treated. 10 months later, he has residual, mild weakness of right deltoid. *Salmonella typhi* has been associated with Guillain-Barre syndrome, and can have neuropsychiatric manifestations. The association with a post-infectious polyneuropathy has not previously been reported.

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**Poster session THUR, 219**

Myopathic manifestations in haematological conditions

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Neurological complications of haematological malignancies are wide ranging but isolated myopathy as a presenting complaint is rare.

**Cases:**

- **63 year-old lady** with progressive proximal upper then lower limb weakness over 7 years to wheelchair-dependence and hoist-transfers. Muscle biopsy revealed nemalin rods, HIV negative, IgG kappa paraprotein=6g/L. Late-onset nemalin rod myopathy was diagnosed; function is stable 6/12 post-autologous bone marrow transplant.
- **56 year-old lady** with limb-girdle weakness leading to immobility over 2 years and IgG lambda MGUS. Re-examination of muscle biopsy revealed amyloid deposition, SAP scan negative for systemic AL amyloid. Treated with velcade and dexamethasone but died from amyloid cardiomyopathy 6/12 later.
- **73 year-old man** with painless deltoid weakness. Muscle biopsy revealed plasma cells infiltrate and lightchain deposition with matched lightchain restriction in bone marrow, IgG kappa paraprotein=8g/L. Cyclosporin and dexamethasone were recommended for infiltrative multifocal, myopathic plasmacytoma.
- **28 year-old female** with pain, fatigue and pelvic-girdle weakness was diagnosed with haemophagocytic lymphohistiocytosis without systemic lymphoma or connective tissue disease. Muscle biopsy demonstrated T-cell and macrophage infiltration. Muscle symptoms are responding to steroids, mycophenolate, cyclosporine and etoposide. An allogenic bone marrow transplant is planned.

We describe four cases of progressive myopathic weakness as the primary manifestation of an underlying haematological disorder.

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Peripheral T-cell lymphomas (PTCLs) are rare and heterogeneous haematological malignancies that can rarely develop first in the peripheral nervous system, or more commonly, invade nerves from more usual primary locations. Patients with PTCLs usually respond poorly to treatment and have a poor clinical outcome.

We report a patient with multiple skin lesions, multifocal mononeuropathies and constitutional symptoms all suggestive of a lymphoproliferative disorder, in whom repeat skin biopsies and clonality studies failed to achieve a diagnosis. Neurophysiological studies confirmed severe post-ganglionic lesions in the lower limbs including the sciatic, femoral, obturator, tibial and sural territories. Based on this neurotropic presentation we undertook a sural nerve biopsy, despite the clinical and neurophysiological presence of a nerve lesion more proximal to the biopsy site, and this allowed us to establish a final diagnosis of PTCL. The patient was treated successfully with chemotherapy and an autologous stem cell transplant.

In our case PET imaging and MR neurography provided radiological evidence of widespread lesions in the subcutaneous and nerve tissues, and there is emerging evidence for the importance of PET imaging in the diagnostic work-up of PTCLs. Furthermore, a post-treatment PET scan confirmed the complete metabolic remission, highlighting its usefulness as a surveillance tool.

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Poster session WED, 222
Hawkes sign: a novel test for carpal tunnel syndrome

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Background: In carpal tunnel syndrome (CTS) patients often report symptoms when elevating the arms, as in driving or phoning.

In Hawkes test both forearms are squeezed firmly about 50mm (2 inches) proximal to the patient’s wrist while simultaneously elevating the subject’s hands just above shoulder height. When positive there is tingling in a median nerve distribution within a few seconds.

Methods: Fifteen patients with suspected CTS were evaluated by a) Tinel’s, Phalen’s and Hawkes’ manoeuvres b) routine nerve conduction tests (NCT) then graded positive or negative and compared with NCT.

Results: Positive signs were present for Tinel in 14/15; Phalen in 8/10 and Hawkes in 15/15. NCT supported CTS in 9/15. Where NCT were abnormal Tinel and Hawkes signs
were always positive but Phalen was negative in 2/7. Where NCT was normal (6/15) the negative/positive rates were: Tinel 1/5; Phalen 3/3; Hawkes 0/6.

Conclusion: All three procedures, particularly Tinel and Hawkes had a high positive rate for CTS, but confirmed by NCT in only 6/15. However, NCT may be falsely negative especially in mild cases. The proposed arm elevation/compression test permits useful initial assessment of CTS although the false positive rate is probably high.

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**Poster session WED, 223**

Predicting disease activity in inflammatory neuropathies

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Background: There is currently no accurate way to determine who will need long-term immunoglobulin (IVIg) treatment in chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN).

Aims: Retrospectively compare clinical, investigational and treatment factors in patients who have successfully ceased IVIg with patients who have active disease.

Methods: 15 patients who have successfully suspended IVIg infusions were compared with 15 in whom decreasing the IVIg dose was unsuccessful.

Results: 30 patients (12 with CIDP and 3 with MMN in both groups) were diagnosed 39.5 months from onset of symptoms in the successful group vs. 40.7 months in the unsuccessful group (p=0.953). There was a significant difference in the summed upper limb sensory amplitudes on electrophysiology prior to starting IVIg between the patients with CIDP (17.4 mV vs. 9.8mV p=0.007). There was no difference between the average doses between the groups. A successful cessation trial was attempted at a mean of 60.5 months post starting treatment, compared with 60 months in the unsuccessful patients.

Conclusion: Other than the differences in initial upper limb amplitudes, other factors did not help predict a successful cessation trial of IVIg. This reinforces the need for an objective biomarker to measure disease activity.

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**Poster session WED, 224**

Building causality networks for inherited neuropathies

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Background: Inherited neuropathies are genetic conditions affecting the peripheral motor and sensory nerves. The number of causative genes are continuing to expand. As more genes are being discovered, more phenotypes are attributed. Despite our rapidly growing knowledge, inherited neuropathies remain incurable diseases.

With the wealth of information now available, bioinformatic platforms are available to visualise functional enrichment of genes and gene-phenotype annotations to enhance our understanding of the mechanism of disease and support hypothesis-driven research.
Methods: The interactors of inherited neuropathy genes were explored using the Search Tool for Recurring Incidences of Neighbouring Genes (STRING) database. Drug-phenotype interactions were assessed using PhenogramViz, human phenotype ontology terms (HPO). We used the Drug Gene Interaction Database (DGIdb) to find drug-gene interactions then used DoGSiteScorer to view potential drug binding pockets.

Results: Inherited neuropathy genes were associated with gene ontology terms related to axonal transport. A total of 380 HPO terms were annotated to the genes which shared a phenotypic spectrum with neurodegenerative disorders. We identified 221 drug-gene interactions.

Conclusion: Bioinformatic platforms are available to rapidly visualise and explore large gene-sets. Platforms to annotate drug-gene interactions need to be developed to assist drug discovery and identify potential agents that can be repurposed.

Poster session WED, 225
Changing epidemiology of motor neurone disease in Scotland
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Clinical Audit Research and Evaluation for Motor Neurone Disease (CARE-MND) (formerly the Scottish MND Register) is an electronic platform for prospective, population-based research in Scotland. We present the results of recent epidemiological analyses.
Capture-recapture methods were adopted to determine incidence of MND in 2015-16: 1) notifications via CARE-MND, 2) Information Services Division (ISD) data i) hospital admissions, ii) death data, iii) riluzole prescriptions.
Crude prevalence of MND in Scotland is 7.61-7.64/100,000 of the population. Direct age standardised incidence in 2015 was 3.42/100,000 (95% CI 2.99-3.91); in 2016, 2.89/100,000 (95% CI 2.50-3.34). Using maximum likelihood estimates, coverage of the CARE-MND platform was 99.6% (2015) and 98.1% (2016). In view of high coverage, CARE-MND estimates alone will be presented for 2017.
Previous Scottish MND Register capture-recapture annual incidence estimates were 2.32/100,000 (95% CI 2.26-2.37) in 1989-1998 (direct standardised). Our data suggest a changing landscape of MND in Scotland, with a rise in incidence by 36%. This could be attributed to improved neurological services in Scotland. Incidence is also 67% higher than Northern European estimates, which perhaps reflects our robust ascertainment methods. However, further work using population CARE-MND data aims to determine if genetic or environmental variables account for these findings.
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Poster session THUR, 229
Inertial sensors improve traditional gait monitoring in HSP patients
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Background: HSP is characterised by spasticity and progressive gait impairment. There’s no reliable way to monitor gait deterioration during clinics. Optoelectronic systems have demonstrated differing characteristics between gait of HSP patients and controls. They’re expensive and impractical for use in clinic settings. Inertial sensors haven’t been used to characterise HSP gait.

Objectives: Study use of inertial sensors to identify gait characteristics that differentiate mild HSP patients from controls. To identify a gait based biomarker which can be used to monitor disease progression in a longitudinal study.

Methods: neurological examination, SPRS, Modified Ashworth score, brief pain inventory were undertaken. Instrumented timed up and go (iTUG) and instrumented 10 metre walk tests (i10) wearing an inertial sensor during clinic appointments at 6-month intervals.

Results: gait variables differentiating between patients and controls, including those with mild disease, were identified. Parameters differentiating between patients with SPG4 and SPG7 mutations were found. 8 patients were re-assessed after 6 months. Analysis did not show gait deterioration.

Conclusion: inertial sensors can detect differences between HSP patients and controls, including those mildly affected. They can also differentiate between patients with different mutations. Further follow up data is needed to assess whether inertial sensors can predict future gait deterioration.

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Poster session THUR, 231
Developing a new rating scale for Ocular Myasthenia Gravis


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Ocular Myasthenia Gravis (OMG) causes ptosis and diplopia, which can be disabling. For this study, OMG is defined as MG patients who have ocular symptoms only and no generalised involvement.

A robust way of assessing the severity of OMG symptoms is important for research, to assess treatment and outcome. The rating scales recommended for MG research have a predominant focus on generalised disease, and are insufficiently sensitive for OMG due to the limited number of ocular questions.

This study aims to create a new rating scale for OMG that is sensitive, reliable and clinically usable. We present our proposal of such a rating scale, which incorporates physician- and patient-rated components.

We report the preliminary results of this pilot observational cohort study, in 60 patients with OMG. We compare the results of this with the MG composite scale.

Future work is planned to validate this rating scale and to develop this alongside the MG Impairment Index (MGII).

For future phases of this study we plan to assess the usability of this rating scale by Neurologists without specialist Neuro-ophthalmology.

We invite feedback from Neurologists at the ABN.
Poster session WED, 236
Skeletal muscle channelopathies and sudden infant death syndrome
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Background: Skeletal muscle channelopathies are rare genetic disorders causing periodic paralysis and myotonia. They are generally considered debilitating but not life-threatening. However cases of life-threatening respiratory muscle crises have recently been reported in infants requiring ITU support. We hypothesised muscle channelopathy gene variants may contribute to the risk of sudden infant death.

Methods: We analysed the SCN4A gene for rare variants in 278 cases of sudden infant death (SIDS) and 729 ethnically matched controls. Biophysical characterisation was performed using a heterologous expression system.

Results: Four of the 278 SIDS cases (1.4%) had an ultra-rare, functionally disruptive SCN4A variant compared to 0/729 ethnically matched controls (p = 0.0057). The degree of channel perturbation associated with these four variants was qualitatively similar to the SCN4A variants previously implicated in infants with life-threatening apnoeic events.

Conclusions: Rare SCN4A variants that directly alter channel function occur in sudden infant death cases. These variants are predicted to significantly alter muscle membrane excitability compromising respiratory and laryngeal function. Data on pregnancy/postnatal complications is now being collected from parents with genetically confirmed sodium channelopathies via clinic and on-line registry. Laryngospasm has recently been implicated in SUDEP - analysis of SCN4A variants in SUDEP cases is also underway.

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Poster session WED, 237
Phosphorodiamidate morpholino oligomers for treatment of Duchenne muscular dystrophy
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Exon skipping is a novel, mutation-specific approach to treating patients with Duchenne muscular dystrophy (DMD). Phosphorodiamidate morpholino oligomers are nucleic acid analogues that selectively redirect pre-mRNA splicing to enable production of internally truncated dystrophin.

In exon 51 skipping (eteplirsen; n=36) and exon 53 skipping (golodirsen; n=25) clinical studies, internally shortened dystrophin mRNA was observed in all treated patients (per reverse transcription polymerase chain reaction). Eteplirsen increased dystrophin expression 15.5-fold, 11.6-fold, and 2.4-fold vs untreated controls (percent dystrophin-positive fibres, Western blot, and immunohistochemistry intensity, respectively; all,
Golodirsen increased dystrophin expression 10.7-fold (Western blot) over baseline following 48 weeks of treatment. Over 4 years, versus comparable external controls, eteplirsen slowed ambulatory decline (6-minute walk test difference, 165 m; P=0.001) and cumulative risk of losing ambulation (83% vs 17%). In 2 clinical studies that included non-ambulatory patients, eteplirsen slowed pulmonary decline versus natural history data (assessed by spirometry).

Eteplirsen and golodirsen demonstrated clinical and biochemical effects in patients with DMD; ongoing studies of these compounds are further characterising their effects in various patient populations.

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**Poster session WED, 238**

Do we follow the ABN myaesthenia guidelines?

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Background: The ABN treatment guidelines (1) for myasthenia Gravis (MG) have recently been published.

Aim: We reviewed the records of patients with MG to assess how well the ABN guidelines are being followed in a district general hospital based neurology centre.

Method: patients: all patients who had positive anti-AchR antibody tests from 2014-17 and clinicians were asked to identify further patients. Retrospective review of electronic patient record, clinic letters and laboratory data reviewed.

Results: 59 patients; 24 ocular and 35 generalised (by type - II: 17, III:15, IV:1, V:1, unclear:1). 63% male, average age 64 (range 18-91).

22/35 (62.8%) generalised MG patients were in remission off pyridostigmine. 13 on steroids, 17 azathioprine, 5 mycophenolate; 3 methotrexate. 2 patients were admitted to ITU, 16 patients had inpatient admissions, 11 patients had IVIG.

14/24 (58.3%) with ocular MG were in remission off pyridostigmine; 5 on steroids, 6 azathioprine. 2 patients had been admitted.

7 of 23 patients on AZT (30.4%) did not have a TMPT level recorded, with only 19 (79%) having sufficiently regular bloods monitoring.

Discussion: Treatment for most patients followed the ABN guidelines. The most common difficulties related to testing for TMPT & blood monitoring.


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**Poster session WED, 240**

An Audit of unplanned admissions in myasthenia gravis patients

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Background: Unplanned admissions of neuromuscular patients adversely affect patients and NHS. Muscular dystrophy UK designed an audit of unplanned admissions of neuromuscular patients in 2012 and 2017.

Aim: We aimed to compare unplanned admissions amongst myasthenia gravis (MG) patients, in two different hospitals in Wessex, Southampton general hospital (SGH) and Queen Alexandra service (QAH).

Methods: Data was collected from patients attending neurology clinics in conjunction with hospital database.

Results: 240 adult patients were included in the audit. 60 unplanned hospital admissions were identified, but only 22 (37%) were judged to be potentially avoidable. 8 admissions were due to myasthenia relapse, 8 occurred in patients with severe myasthenia on dual immunosuppression. 9 admissions were due to pneumonia in elderly patients with multiple comorbidities but well controlled myasthenia. 2 admissions were anxiety related and 3 were due to falls and fracture despite appropriate bone protection.

Conclusion: Our preventable admission rate for MG patients is less compared to MDUK data (37% vs 68.7% and 59.4% in 2012 and 2017). Pneumonia is common in elderly myasthenic patients who have other comorbidities. Fragility fractures can occur despite bone protection and falls advice is necessary during consultation.

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Poster session WED, 241
Clinical relevance of regular blood monitoring in Ig treatment

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Background: ABN immunoglobulin (Ig) guidelines advise routine FBC and U&E monitoring with every treatment episode and screening for IgA deficiency.

Aims: We audited compliance in inflammatory neuropathy patients on longterm treatment in two UK Neurology departments. We looked for evidence of clinically relevant haematological or AKI Ig-related events.

Methods: Data was collected from Nov 2015 to Nov 2017. Accepted definitions for clinically and/or biochemically significant haemolysis, neutropenia, thrombocytopenia and AKI were used.

Results: 1919 treatment episodes in 90 patients were analysed. Mean age(S.D)= 57.6(14.4) years, 69.1% male, 74% CIDP (26% MMN), 94% IVIg (6% SCIg). Mean dose= 1.57 (0.74) g/kg/month or 97.1(37.3)g/infusion. No clinically significant episodes of haemolysis, neutropenia, thrombocytopenia or AKI occurred in relation to Ig treatment. An asymptomatic drop of >10g/L Hb occurred in 68/1919 episodes in 38 individuals (3.5%); mean reduction 17.7 g/L, lowest Hb 99g/L. Two patients with CRF (stage 3) received 28 (IV) and 104 (SC) infusions respectively without impact on eGFR. Two individuals with relative IgA deficiency (0.38g/L, 0.4g/L) received 16 infusions over 1.5 years without complications.
Conclusions: No clinically significant Ig-related events were identified in this representative cohort. We suggest annual screening or clinically indicated testing as safe and more appropriate in longterm IVIg use.

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**Poster session WED, 242**

A challenging case of periorbital swelling

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A 54 year old lady was referred with a eighteen month history of slowly progressive, asymmetric, periorbital and facial oedema. She was thought to have inflammatory orbital pseudotumour. During this time, she had also developed a dry mouth, joint pains and enlarged salivary glands. A salivary gland ultrasound scan was suggestive of Sjogren’s disease although antinuclear antibody and rheumatoid factor were negative. She had recently been prescribed omeprazole for mild dysphagia and hoarse voice from vocal cord oedema.

Past medical history included Hashimoto thyroiditis for which she was taking levothyroxine.

Clinical examination revealed peri-orbital and facial oedema causing proptosis of the right globe and complete lid closure. Visual acuity, eye movements and visual fields of the left eye were normal. Her voice was hoarse and she had mouth ulcers. She had a widespread erythematous rash that was thought to be a drug reaction to omeprazole.

Apart from mild lymphopenia and mildly deranged liver function, blood tests, including inflammatory markers and thyroid function, were unremarkable.

MRI of the brain and orbits revealed diffuse oedema of facial structures, including the orbital muscles. A CT body scan was unremarkable.

A temporalis muscle biopsy confirmed a high grade NK/T cell lymphoma.

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**Poster session WED, 243**

Enhancing our knowledge of leptomeningeal disease – a case of DL-GNT

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A 57-year-old woman presented with several weeks of headache associated with neck stiffness, drowsiness and nausea. She developed diplopia with right-sided 6th nerve palsy and subsequently developed a complex opthalmoplegia and right-sided ptosis.

Repeated lumbar punctures showed high opening pressures of up to 60cm H2O and high protein levels up to 2.48g/L. She developed episodes of marked loss of responsiveness but EEGs showed only generalised slowing. Brain imaging was essentially normal. An MRI Spine showed an enhancing intramedullary hyperintensity T8-T10 with overlying
meningeal enhancement. A CT-PET scan revealed uptake along the cord consistent with diffuse infiltration or a meningitis – biopsy was inconclusive but macroscopically the dura was thickened with calcification observed on the spinal cord surface. A brain biopsy did not aid diagnosis and unfortunately the patient deteriorated with increasing severity of headaches and drowsiness. She died after a number of cardiorespiratory arrests.

At post-mortem, thickened meninges showed a glioneuronal cell infiltrate and a diagnosis of diffuse leptomeningeal glioneuronal tumour (DL-GNT). WHO recently described DL-GNT in the 2016 update of CNS tumour classification. Previous case reports of this rare disease have concerned adults and children. DL-GNT should be considered in cases of radiological leptomeningeal enhancement and high CSF protein levels.

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Poster session WED, 244
CSF cytology alone is unable to predict CNS neoplastic process

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Incidence of both primary and secondary central nervous system (CNS) malignancies are increasing, yet detection and diagnosis of which remains challenging. Neurological examination, CSF cytology and neuroimaging each offer diagnostic value, however, individually, each method has relatively low sensitivity. CSF cytology is often routinely requested as part of the diagnostic work-up. Therefore, we reviewed the value of CSF cytology in predicting CNS neoplastic process.

We systematically analysed 296 patients who had had CSF cytology. All consecutive patients over the last 2 years were included. The 12 patients positive for CSF cytology were also found to have concurrent; clinical findings (92%), radiological findings (92%), or both (83%). In no patient CNS malignancy was identified by CSF cytology alone. Additionally, only 7 of the 12 CSF positive cases were collected by means of lumbar puncture, the rest were carried out during neurosurgical procedures.

We conclude that if there is neither clinical findings nor abnormal neuroimaging, assessing CSF cytology does not contribute towards diagnosis of CNS malignancy. Yield of CSF cytology is high when both clinical and radiological evidence are present. Where neuroimaging is normal but suspicion remains, the low sensitivity of the CSF-cytology would make it a weak corroborator to exclude malignancy.

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Poster session WED, 253
An atypical presentation of Sneddon syndrome

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A 50-year-old female was admitted following a subacute and increasing headache, numbness in both hands and feet, generalised weakness and confusion. An MRI brain revealed an acute left temporal infarct with multi-focal established infarcts. MR angiography demonstrated marked occlusive disease affecting terminal internal carotid
artery and both middle cerebral and posterior cerebral arteries, in a potential Moyamoya pattern.

Lumbar puncture, extensive blood tests and echocardiography were unremarkable.

A skin biopsy showed intimal thickening of the deep dermal arteries compatible with a diagnosis of Sneddon Syndrome. Livedo reticularis was absent and antiphospholipid antibodies negative.

Antiplatelet therapy only was commenced given her seronegativity and Moyamoya.

Discussion: Sneddon syndrome is an uncommon disorder, characterised as generalised livedo reticularis with stroke (Sneddon, 1965). It is an increasingly recognised cause of ischaemic stroke in young adults, however, its clinical course remains poorly defined in the literature (Boesch et al 2003). It is increasingly associated with Moyamoya syndrome, posing a challenge in terms of anticoagulation in these patients (Fierini et al 2015). To our knowledge, this is only the second reported case without livedo reticularis (Marianetti et al 2011) - highlighting the importance of skin biopsy - and the first with this clinical and radiological combination.

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**Poster session WED, 255**

SSRIs and Risk of Intracerebral Haemorrhage

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The abstract has also been presented as an oral presentation at the ESOC conference.

Background and Aims: Observational studies have suggested increased risk of intracranial haemorrhage (ICRH) in patients receiving selective serotonin reuptake inhibitors (SSRI). We sought to clarify the impact of SSRI on ICRH, accounting for study methodology.

Method: A comprehensive search of Medline, Embase and Cochrane from 1960 to December 2017 comparing SSRI with control. ICRH was meta-analysed using a random-effects model and the review was prospectively registered (PROSPERO:CRD42017084513).

Results: 25 observational studies, but no randomised trials, were available for meta-analysis, with a combined total of 4,843,857 patient-years follow-up. Those treated with SSRI were more likely to have depression (p<0.001) and be female (p=0.04). Compared to control, SSRI were significantly associated with first-ever ICRH (RR 1.31, 95% CI 1.15-1.49); however, in survivors of ICRH there was no association between SSRI and recurrence (0.95, 0.83-1.09). Sensitivity analyses revealed a greater association between SSRI and ICRH in studies with a high risk of bias (p<0.001) than those with a lower risk of bias (p=0.10).
Conclusion: SSRI are associated with increased risk of first-ever ICrH, but not with recurrence. These findings, based solely on observational data, should be taken with caution due to fundamental differences in patients receiving treatment, highlighting the need for randomised trials.

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**Poster session WED, 258**

Stroke mimic diagnoses on a centralised hyperacute stroke pathway

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Introduction: Stroke is highly prevalent, with an estimated 25.7 million occurring worldwide in 2013. Stroke outcomes in the UK are poor by international standards. In an effort to reduce mortality and length of hospital stay, hyperacute stroke services have been fully centralised in Greater Manchester since 2015 such that all possible strokes within 48 hours of onset are transferred for assessment at one of three stroke centres. However, there have been concerns regarding the transfer of stroke mimic diagnoses along such pathways.

Methods: A retrospective analysis was performed of patients assessed by the hyperacute stroke team in the Emergency Department of the Comprehensive Stroke Centre (Salford Hospital) in December 2015.

Results: In December 2015, 309 patients with queried stroke were assessed by the Comprehensive Stroke Centre hyperacute stroke team. Of these, 82% had been redirected or transferred from another hospital. 47% had a non-stroke diagnosis at discharge or repatriation, resulting in a combined 331 days of stay at Salford hospital by patients without a stroke. The five most common non-stroke diagnoses were TIA, migraine, infection, seizure and functional neurological disorder.

Conclusions: The optimal clinical care of non-stroke patients should be considered when planning centralisation of hyperacute stroke services.

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**Poster session WED, 259**

The challenge of mood and cognition screening in HASU

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The National Clinical guideline for stroke, recommends that services for people with stroke should provide screening for mood and cognition within six weeks of stroke using validated tools. In HASU assessing mood and cognition in a timely fashion has been challenging. In 2013 a previous audit showed cognitive screening at 48% and mood screening at only 7%. We instituted a number of measures to improve compliance including education
events for MDT staff, a bespoke stroke clerking proforma, to include data collection boxes. We also introduced the briefer “YALE questionnaire” for mood, and the Montreal Cognitive Assessment Tool (MOCA). We also piloted occupational therapy staff using a “screening sticker” in patient notes. A daily MDT was also introduced, primarily to improve patient flow, but also to prompt action planning. Mood screening improved to 92% and cognition screening to 95% on detailed notes audit. These high compliance figures were however not fully reflected on SSNAPP although compliance has improved. SSNAP data input is completed by a single coder, non clinical staff member. We plan to employ a second data clerk and further revise the stroke proforma.

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Poster session WED, 260
Time to scan: barriers to imaging outside normal working hours

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SSNAP measures quality and organisation of stroke care. Domain 1.1 looks at the number of patients scanned within 1 hour of arrival at hospital; local trust performance is 57.4% (national average 51.3%), with the specialist stroke unit at 79.2%. This is in part related to "direct to scan protocols" in extended working hours, but we currently lack equivalent medical staffing and radiographer support during this time. We aimed to explore which factors impacted on scanning time out of hours. An initial consecutive 14-day sample identified delays in approval of scan request by the duty radiologist. A new Standard Operating Procedure allowed specialist stroke nurse practitioners (SNPs) to request CT head scans directly with the duty radiographer, eliminating need for liaison with the radiologist. A repeat 14-day analysis identified additional factors resulting in delays, including delays in scan request and in-hospital competing emergency clinical scanning requirements, meaning no significant improvement in percentage of patients scanned within 1 hour was observed. The mean time from arrival to scan performance was 52 minutes, but 21.8% of patients did not undergo a CT head within 1 hour of arrival. Further strategies are required to maximise patients meeting this target.

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Poster session WED, 261
Stroke scan agnosia – what radiologists do not see

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Background: Neuroimaging helps clinicians make accurate diagnoses. Most stroke patients have their imaging reported by general radiologists.

Methods: As part of a quality assurance program a database for neurological patients with second opinion reporting from neuroradiologists was searched from 2008 to 2016 to identify patients in whom stroke lesions were missed at initial reporting by general radiologists. Patient demographics, scanning modality, stroke type, location and laterality were recorded.
Results: 36 patients, 18 men, 18 women, mean age 59.0 (SD 13.8) years were identified in whom a stroke lesion was not detected on initial reporting. The lesions included cerebellar infarcts in 14 patients (bilateral in 3), pontine ischaemia/infarction (n=6), supratentorial infarction (n=9), vessel abnormality (n=6 – dense middle cerebral and basilar arteries, dissection and cerebral venous sinus thrombosis), and spinal infarction (n=1). In 9 (24%) patients the missed lesions occurred solely on CT brain scanning. The missed lesions were acute presentations in 8 (22%) patients.

Conclusion: Stroke lesions can be missed with both CT and MRI. The posterior fossa and dense artery signals (middle cerebral artery and basilar artery) are prone to detection errors.

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**Poster session THUR, 262**

Diagnosis of OSAS in neurology outpatients

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Background: Obstructive sleep apnoea syndrome (OSAS) can present with neurological symptoms. Treatment of underlying OSAS can improve neurological comorbidities like Parkinson’s, epilepsy and Alzheimer’s. Early identification of OSAS may explain and improve symptoms. The aim of this study was to identify the association between the diagnosis of OSAS and presenting symptoms like headaches, memory problems, seizures and vertigo.

Methods: The medical records and polysomnography reports of 40 patients, newly diagnosed with OSAS by a consultant in a neurology outpatient clinic at a NHS district general hospital, were reviewed; the likelihood of OSAS explaining presenting symptoms was rated on a 1-4 scale.

Results: 32 OSAS patients were included in the study (21 male and 11 female). 15 patients (46.8%) presented with headaches, 5 patients (15.6%) with memory problems, 5 patients (15.6%) suffered from (dissociative and epileptic) seizures and 1 patient (3.1%) suffered from vertigo. 10 patients (31%) newly diagnosed presented with none of these neurological symptoms. All 32 patients presented with at least one of the typical symptoms of OSAS for example daytime sleepiness, snoring, and witnessed apnoeas.

Conclusion: Undiagnosed OSAS is likely common in neurology outpatients and often can explain presenting symptoms and can be a treatable co-morbidity.

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**Poster session THUR, 263**

5 year review of our specialist obstetric-neurology clinic

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Introduction: The confidential enquiry into maternal deaths has shown that neurological disorders are the second most frequent cause of indirect maternal death and lack of access
to a specialist service was the main factor contributing to the number of preventable deaths.

Method: We looked at our local joint neuro-obstetric clinic over a 5 year period and studied the number of patients seen each year, the diagnosis, list of current medications and the referral route.

Results: The numbers of new patients seen in the clinic each year increased from 27 in 2013 up to 62 in 2017. Epilepsy was the commonest presentation, followed closely by migraines and then multiple sclerosis. With regards to medications, a third of epileptic patients were on dual anti-epileptic therapy and there were still patients taking sodium valproate at presentation. Initial referrals to the clinic were mainly from the local midwife-lead antenatal service. More recently, there has been a significant increase in referrals from the local neurology service and other allied specialties.

Conclusion: This data confirms that the number of patients seen in our service has more than doubled over the 5 year period, largely as a result of increased awareness of our easy-to-access multi-disciplinary clinic.

Poster session THUR, 264
Multimodal intervention to improve lumbar puncture

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Introduction: Lumbar puncture (LP) is a routine procedure performed for diagnostic and therapeutic indications for more than 120 years. For as long, post-dural puncture headache (PDPH) has been a complication that can be persistent and severe. Finer gauge needles and ‘atraumatic’ needle designs significantly reduce the incidence of PDPH.

Methods: A multimodal intervention consisting of teaching session on atraumatic needle usage, simulation training with 25G Sprotte needles, and electronic LP proforma was introduced in October 2017.

Records for all patients having LP in the Neurology day-case unit at the John Radcliffe Hospital, Oxford, in the months of November 2016 and Nov/Dec 2017 were retrospectively reviewed for documentation and atraumatic needle usage.

Results: 39 records were reviewed from Nov/Dec 2017 and 16 from November 2016. Documentation was significantly improved across all criteria assessed except for documentation of informed consent. Atraumatic needle usage increased from none documented pre-intervention to 38% (n=11 out of 29 where atraumatic needle indicated) post intervention.

Conclusion: Proforma use was associated with improved LP documentation. Atraumatic needle usage increased significantly post-intervention. These results are consistent with previous studies on changing behaviour in LP technique in neurology. Large scope for further improvement exists.

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Poster session THUR, 265
Complaints from patients with functional disorders
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Objective: To evaluate the nature of complaints from patients with functional neurological disorders and understand the reaction of UK neurology consultants to receiving complaints from this patient group.

Methods: A voluntary anonymised online retrospective survey was advertised to UK consultant neurologists. Questions asked about the nature of the complaint, how it was dealt with, how it affected their emotional wellbeing, attitude to work, and whether it influenced their clinical practice. The frequency of total responses was analysed. Respondents were given opportunities to add comments.

Results: Responses from 58 clinicians were included. The majority of complaints stemmed from patients not agreeing with their diagnosis. Complaints from patients with functional disorders tended to be more involved and personal than other complaints. Lack of awareness about functional conditions among non-specialists was also a common theme. For many respondents, the complaint adversely affected their emotional wellbeing. Following the complaint, defensive practice was more common, and working patterns were altered.

Conclusions: Complaints from patients with functional neurological disorders appear more difficult to resolve than other complaints, and clinicians who deal with them often become the ‘second victim’ in the process leading to potentially adverse effects on patient care. Strategies to tackle these issues are discussed.

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Poster session WED, 268
Improving junior doctors induction: Queen Square junior doctors handbook

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Introduction: All junior doctors joining Queen Square undergo an induction package delivered along with the Queen Square Junior Doctors’ Handbook (QS-H). QS-H is supposed to provide general guidance to daily medical jobs in addition to useful clinical information, contact details and hints.

Aim: The aim of this quality improvement project (QIP) was to update, and improve, the quality of QS-H. The idea was that better and more informative induction can make carrying out daily jobs easier, increase the efficacy/effectiveness of medical staff and, ultimately, impact positively on patients care.

Methods: In this QIP a participatory assessment approach was employed where the opinions of the beneficiaries (junior doctors) were sought to screen for the strengths/weaknesses of the old version of QS-H, and to assess, later on, the new version.

Results and conclusion: Most junior doctors highlight the length of QS-H and the outdated information of its contents. Based on their suggestions a new, brief and practical version was drafted and was well received with some comments that led to additional round of improvement. Distributing hardcopies of QS-H around the wards further improved the junior doctors’ accessibility, efficiency, effectiveness and satisfaction.

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**Poster session WED, 270**  
Optician’s diagnosis of papilloedema impact hospital admissions  
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Background: In a landmark case in August 2016 an optometrist was found guilty of missing papilloedema. We examined the current referral pathway for managing papilloedema to determine whether initial assessment by an optician impacted resource use.  
Methods: Discharge summaries from St Marys Hospital (SMH) between 1/1/17 and 16/5/17 the referral centre for the Western Eye Hospital (WEH) accident and emergency (A&E) were searched to identify subjects with suspected papilloedema. Analysis of the patients journey was performed.  
Results: Of 76 patients identified, 26 were excluded either due to being <18 years old or were treated elsewhere. Of the 50 included, 25/50 were seen by an optician prior to a WEH A&E ophthalmologist, 75% of these were referred for urgent hospital assessment with an admission rate of 45.8%. Of 19/50 assessed by WEH A&E only there was a significantly lower urgent assessment referral rate (75% vs 52.6%, p=0.02) and admission rate (45.8% vs 21%, p=0.02). Of the 6/50 patients finally found to have normal discs, 5 were initially referred by opticians.  
Conclusion: Referral by optician prior to ophthalmology A&E assessment is more likely to result in rapid referral for urgent hospital assessment and inpatient admission.  
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**Poster session WED, 273**  
Wessex HealthLines: Neuroline  
Lillistone Pauline¹, Chappell Rachel¹, Dukes Charlie², Higenbottam David², Kipps Christopher¹,²,³  
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Background: The ability to provide timely signposting to patient with neurological conditions seen in clinic is crucial, but information resources are not always available or updated. Individuals wishing to participate in clinical trials may find it difficult to locate research opportunities, and busy clinicians may not be aware of local clinical research studies. We sought to develop a means of collating, organizing and displaying information on neurological conditions and research trials in an easily accessible form online.  
Methods: Over 350 local support groups, information resources and websites dealing with neurological conditions relevant to neurological patients in Wessex were identified. These were then displayed via a website that maps these resources, and offers a summary with a link to the primary source.  
Results: Over the past year, the Wessex HealthLines site has been visited by over 2300 users, with the NeuroLine pages (wessexhealthlines.nhs.uk/neuroline) accessed by over
750 users. The site has now been expanded to include neurological research trials running in the region (ResearchLine).

Discussion: The Wessex HealthLines website (NeuroLine, ResearchLine) makes use of multiple resources to support information signposting in neurological conditions, and to clinical trials, across Wessex. Other regions interested in quality improvement projects may find this approach useful.

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**Undergraduate Prize Winner 2018**

Exome analysis to investigate autosomal dominant vasovagal syncope

Aaron Jesuthasan, Dr. Michael Keogh, Prof. Patrick Chinnery

INTRODUCTION: Vasovagal syncope (VVS) is the most common cause of syncope in children and adults. Previous studies suggest a genetic component accounts for approximately 20% of cases, although the genes responsible are often unidentified. I studied the DNA of two distantly related individuals with VVS enrolled into the 100,000 Genomes Project to identify causal mutations.

METHOD: DNA was extracted from the patients, and analysed using an Ingenuity Variant Analysis program to detect the presence of mutations. The severity of each detected mutation was subsequently examined using two programs: Sorting Intolerant from Tolerant (SIFT) and Polymorphing Phenotyping v2 (PolyPhen-2).

RESULTS: Using Ingenuity Variant Analysis, a mutation in the **ACE** (*Angiotensin Converting Enzyme*), **EPAS1** (*Endothelial PAS Domain Protein 1*) and **PLCG2** (*Phospholipase C Gamma 2*) genes of the VVS patients were identified. Further analysis using SIFT and PolyPhen-2 indicated the **ACE** mutation was likely to produce a defective protein whilst the **EPAS1** and **PLCG2** mutations were unlikely to have any effect on protein function.

CONCLUSION: My results support the involvement of the **ACE** mutation in the cause of VVS within the two studied patients. This may point towards a novel target for therapy within the individuals, should the findings be successfully validated.

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**Poster: Acute Neurology Care Model – “The Neuro Network”**

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The neuro network is a well-developed model in North West England and North Wales, hosted by the Walton Centre Liverpool. It is based on the principle of an equitable, locally accessible service taking responsibility for a regional population, rather than one based on a single unit or small area.
Centralised tertiary activity is based in Liverpool – for patients requiring specialised diagnostic or therapeutic intervention and care; particularly neurosurgery, thrombectomy, neurological ITU or frequent review of complex acute neurological disorders.

Acute neurological support is delivered to 12 acute sites across the region using a combination of consultant visits and ward liaison sessions (typically 3-4 days each week), telemedicine video consultations (presently being developed at pilot sites), 24/7 telephone advice and a weekday consultant advice line for GP’s. Patients are then treated, whenever possible, by a local medical team (or HASU) supported by a neurology management plan (and subsequent on-site or remote review if necessary) or by transfer to the centre if clinically appropriate.

The model offers acute neurology provision to a wide area, by the most effective, resilient and equitable deployment of limited resources.

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**Platforms**

**Case presentation competition, 0900**

A new face for an old foe?

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Background: Mutations in the protein gelsolin result in hereditary systemic amyloidosis, characterised by onset of corneal lattice dystrophy in the third decade, a slowly progressive cranial neuropathy and cutis laxa. To date four dominantly inherited gelsolin mutations have been identified, two mutations resulting in the classical syndrome and two mutations resulting in renal-predominant amyloidosis.

Methods: We identified a family in which four individuals in three generations presented with corneal lattice dystrophy and neurological symptoms. Detailed clinical neurological and ophthalmological assessment and investigations including neurophysiology and imaging were performed. Whole exome sequencing was undertaken in three family members.

Results: Whole exome sequencing revealed a novel variant in the gelsolin gene (c. G1738A; p. E580K), dominantly inherited and predicted to be pathogenic. Examination, neurophysiological testing and imaging revealed the presence of distal upper limb weakness and wasting, corneal lattice dystrophy and cervical myelopathy in all affected family members.

Conclusion: The E580K mutation described in this family is in a conserved calcium-sensitive actin-binding domain that displays sequence homology with other actin-depolymerising proteins. Mutations in this domain may result in abnormal gelsolin-actin interactions and changes in calcium sensitivity may render the protein susceptible to the same aberrant proteolytic cascade as with other known mutations.

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Case presentation competition, 09.24
Disentangling corticobasal syndrome from corticobasal degeneration

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Mutations in the TANK-binding kinase (TBK1) gene have been shown to cause frontotemporal dementia (FTLD) and amyotrophic lateral sclerosis (ALS). The phenotype is highly variable and has been associated with behavioural variant FTD, primary progressive aphasia and pure amyotrophic lateral sclerosis. We describe the clinical, anatomical and pathological features of a patient with onset of a corticobasal syndrome (CBS)/primary progressive aphasia overlap aged 59. The patient presented with progressive speech difficulties and later developed an asymmetric akinetic-rigid syndrome. Neuroimaging showed asymmetrical frontal atrophy, predominantly affecting the right side. There was a strong family history of neurodegenerative disease with 4/7 siblings developing either dementia or ALS in their 50’s-60’s. Following death at age 71, postmortem examination revealed FTLD TDP-43 type A pathology. Genetic screening did not reveal a mutation in the progranulin, microtubule-associated protein tau or C9orf72 genes. However exome sequencing revealed a novel E703X mutation in the TBK1 gene. Although segregation data was not available, this loss of function mutation is highly likely to be pathogenic. In conclusion, we show that TBK1 can be a cause of an atypical parkinsonian syndrome and screening for TBK1 should be considered in CBS patients with a family history of dementia, ALS or CBS.

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Case presentation competition, 10.00
Inspector NORSE

Ross Russell Amy¹, Massey Luke¹, Williams Imogen¹, Fabian Mark², Nicoll James², Eren Efrem², Pelosi Emmanuela², Prevett Martin², Hell James², Katifi Haider²

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A 26 year old, Caucasian, female student nurse presented with facial pains and vesicular rash, and over the following three days developed focal faciobrachial twitches. She was febrile, with an erythematous rash. Neurological examination was normal. MRI showed a non-enhancing lesion in the right medulla. CSF was normal with negative viral PCR. EEG demonstrated no seizure activity.

A month earlier she was treated with steroids and antibiotics for acute liver injury and maculopapular rash, of presumed allergic aetiology. On that admission, deficiency of Immunoglobulins A and G was noted prompting diagnosis of Common Variable Immune Deficiency, treated with IVIg.
Her conscious level deteriorated rapidly, requiring ventilation 10 days after admission. Repeat MRI showed a new subcortical inflammatory lesion. EEG showed new background slowing, and progressed to electrographic status, which continued despite six anticonvulsants, IV Propofol and Midazolam. Sequential imaging showed progressive deterioration with widespread inflammation and oedema, and consequent herniation. Life-support was withdrawn one month after presentation.

Post-mortem demonstrated T-lymphocytic inflammation with inclusion bodies suggesting viral encephalitis. Electron microscopy demonstrated filamentous viral particles. Measles PCR was positive in brain tissue and CSF, diagnosing Measles Inclusion Body Encephalitis. Serum measles IgM, previously reported as negative, was re-evaluated and tested positive.

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**Parallel session 1: Clinical Neurology, 11.15**

Apraxia and the temporal lobe in action: a role for biological motion

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Limb apraxia is a syndrome that affects the ability to perform skilful actions, despite intact elementary motor and sensory systems. Using voxel-based lesion symptom mapping in a large cohort of 387 stroke patients we determined the neuroanatomy of three tasks traditionally used to study praxis skills in patient populations: these included a meaningless gesture imitation task, a gesture production task involving pantomime of transitive and intransitive gestures and a gesture recognition task, involving recognition of these same categories of gestures. Lesions associated with reduced performance in these tasks involved an integrated network previously described in biological motion, with input areas comprising left pre-striate and occipital regions, left superior temporal sulcus and motor output areas comprising left premotor area, left striatum and the white matter underlying the left primary motor cortex. This study confirms a role for the left hemisphere in limb apraxia and supports the hypothesis it is a white matter disconnection syndrome, whilst shedding new light into the nature of the behavioural deficits described in the disorder comprising parts of an integrated network of brain areas described in biological motion.

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**Parallel session 1: Clinical Neurology, 11.39**

A screening questionnaire for transient loss of consciousness

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Background: Transient loss of consciousness (TLOC) is a common primary care presentation. 90% are due to syncope (S), epilepsy (E), or psychogenic non-epileptic seizures (PNES). Misdiagnosis and delayed diagnosis is common. We explore symptoms and witness observations that can classify patients with likely diagnoses of E, S, or PNES.

Methods: Patients with objectively-documented diagnoses of E, S, or PNES, and an attack witness, were invited to complete a questionnaire (capturing medical history, 86 peri-episodal experiences, and 31 witness observations). Iterative feature selection identified questions strongly predictive of diagnosis; a random forest trained on these classified patients into likely diagnoses of E, S, or PNES.

Results: 249 patients (86 E, 79 S, 84 PNES) were randomly assigned to training or validation in a 2:1 ratio. Feature selection identified 36 highly-predictive questionnaire items. The classifier correctly diagnosed 86% of patients in validation. 100% of S were correctly diagnosed, 85.7% E and 75% PNES. A simpler 12-feature model correctly classified 76.7% of cases (E: 75%; S: 92.3%; PNES: 65.6%).

Conclusions: TLOC-associated symptoms and manifestations can contribute to a decision rule for primary/emergency care, assisting triage and referral. Determining a diagnostic pre-test probability from TLOC features can aid interpretation of investigation abnormalities of uncertain significance.

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Parallel session 2: Mechanisms of disease, 11.15

Predicting neurodegeneration after traumatic brain injury

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Background: Dementia rates are elevated after traumatic brain injury (TBI) and a subgroup develops chronic traumatic encephalopathy. Post-traumatic neurodegeneration can be measured by brain atrophy rates derived from neuroimaging, but it is unclear how atrophy relates to the initial pattern of injury.

Objectives: To investigate the relationship between baseline TBI patterns and subsequent neurodegeneration measured by progressive brain atrophy.

Methods: 55 patients after moderate-severe TBI (mean 3 years post-injury) and 20 controls underwent longitudinal MRI. Brain atrophy was quantified using the Jacobian determinant defined from volumetric T1 scans approximately one year apart. Diffuse axonal injury was measured using diffusion tensor imaging and focal injuries defined from T1 and FLAIR. Neuropsychological assessment was performed.
Results: Abnormal progressive brain atrophy was seen after TBI (~1.8%/year in white matter). This was accompanied by widespread reductions in fractional anisotropy, in keeping with the presence of diffuse axonal injury. There was a strong negative correlation between FA and brain atrophy, whereby areas of greater white matter damage showed greater atrophy over time.

Conclusions: The results show a strong relationship between the location of diffuse axonal injury and subsequent neurodegeneration. This suggests that TBI triggers progressive neurodegeneration through the long-lasting effects of diffuse axonal injury.

Parallel session 1: Clinical Neurology, 11.51
Skull base dural AVF mistaken as cervical myelitis: a series
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Background: Cervico-medullary spinal cord lesions are usually inflammatory (or rarely neoplastic). Dural arteriovenous fistula (DAVF) is considered very unlikely in the cervical cord, particularly if the history is of an acute myelopathy.

Method: Case note review of five patients with skull base DAVF.

Results: All were men aged 60-69 years. Four were symptomatic for a month or less, followed by acute deterioration over hours-7 days, mimicking myelitis. MRIs showed extensive T2-hyperintensity and swelling in the cervico-medullary region. Worsening after corticosteroids occurred in 3/4 patients and one needed ventilation. Conspicuous and unambiguous cord-surface vessels were present in only one patient. Clinical suspicion prompted digital subtraction angiography (DSA) in the other four patients. Median time from initial MRI to diagnostic DSA and embolization was 28 days (7-91 days). All patients survived with good clinical recovery.

Systematic retrospective review of MRIs showed lack of gadolinium enhancement in 4/5. CSF examination (n=4) showed normal leucocyte count in all cases and elevated protein concentration in 3/4 (0.6-1.2 g/L).

Conclusion: Skull base DAVF can mimic acute cervical myelitis. Steroids may prompt life-threatening clinical deterioration mistaken for ascending myelitis. A low threshold for angiography in the context of non-enhancing lesions and acellular CSF will facilitate earlier diagnosis and improve outcomes.

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Parallel session 2: Mechanisms of disease, 12.03
Quantifying muscle amyloid in inclusion body myositis using PET
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Objectives: Inclusion body myositis (IBM) shares some histopathological features with polymyositis (PM). Current investigations have low sensitivity for identification of amyloid deposits that are characteristic of IBM, contributing to frequent misdiagnosis. We compared muscle amyloid content, quantified using a novel positron emission tomography (PET) technique, in IBM and PM.
Methods: Ten cases with IBM and six controls with PM underwent clinical review, [18F]florbetapir PET/computed tomography, and magnetic resonance imaging (MRI) of whole-body skeletal musculature. [18F]florbetapir standardised uptake value ratios (SUVRs, reference = lumbar fat pad) in skeletal muscle were compared between cases and controls. The relationship in IBM of [18F]florbetapir SUVRs to clinical and MRI-derived measures of disease severity were also investigated.

Results: [18F]florbetapir SUVRs were significantly higher in those with IBM for all muscle regions assessed (total SUVR 1.45 [IQR 1.28-2.05] versus 1.01 [IQR 0.80-1.22], p=0.005). Strong negative correlation between MRI-derived muscle inflammation levels and [18F]florbetapir SUVRs were observed only in calf muscles bilaterally (right -0.73, p=0.02; left -0.68, p=0.03). No significant relationship between [18F]florbetapir SUVRs and clinical measures of disease severity were identified.

Conclusion: Muscle amyloid imaging using [18F]florbetapir PET may be useful in the diagnostic workup of IBM, particularly when differentiating from PM.

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Acute neurology platforms, 13.00
Acute Neurology in Aneurin Bevan University Health Board

Joe Anderson

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Aneurin Bevan University Health Board (ABUHB) provides for a population of 640,000 in South East Wales, in addition to South Powys. The large geographical area contains 3 sites with acute unselected medical intake as well as 3 other hospitals. The neurology department, comprising 6 consultants (1 stroke/neurology), 1 associate specialist and 1 trainee, is based in Newport. Service evaluation (2013) revealed that 1 in 6 neurology clinic appointments were used to see patients discharged from acute medicine, with a median waiting time of 14 weeks. In 2015 the “Neurologist of the Week” service was launched; 5 consultants participate on a weekly rota. Routine work is cancelled and replaced with a 10 DCC (~40 hours) acute neurology week. This includes 3 acute clinics (each 3 patients), daily MAU round for the largest site, and a triage and advice service for primary and secondary care. Visits to other hospital sites are made when needed. The service has led to significant improvements in quality of care, neurology training and undergraduate teaching and is highly valued by colleagues. Repeated evaluations show ~55% of acute clinic patients are discharged, with ~40% of appointments preventing or shortening an admission. Diagnosis is significantly changed in ~40% of consultations.

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Acute neurology platforms, 13.05
Piloting and implementing an acute neurology service

Thomas Peukert

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Over the past decade, the number of patients attending the emergency department (ED) at the Royal Victoria Hospital Belfast, with neurological symptoms, has doubled. Typically, over 50% of these patients would subsequently be admitted to hospital. In 2013, a pilot project was conducted with the aim of evaluating the effectiveness of a rapid access neurology clinic on reducing such admissions.

A dedicated neurology clinic was set up offering 12 slots per week. Patients were seen within 10 days of ED staff booking them into the clinics. Early results indicated that within the first month 28 admissions were avoided. As a result rapid access neurology clinics were rolled out. Two acute neurologists were appointed and since 2015, 3 rapid access clinics run per week (15 slots). In addition to the rapid access clinics, the acute neurology team also offer two additional services:

- Reviewing all patients who have been admitted under the medical take with neurological symptoms
- Patients who attend ED overnight but require urgent evaluation/tests can be sent home and will be seen the next morning by the acute neurology team

Analysis indicates approximately 1250 admissions are avoided each year with an estimated cost saving of over £2 million.

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**Acute neurology platforms, 13.10**

Hyperacute stroke unit and hyperacute neurology unit under one roof


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The Acute neurology unit (ANU), located at the Royal Hallamshire Hospital, Sheffield is a regional centre for a population of approximately 1.5 million. We are unusual, as our neurologists manage both hyperacute stroke and hyperacute neurology. HASU is located within our ANU. We had 4026 neurology ward admissions, 3265 emergency cases and 761 elective cases last year. We receive acute admissions from Trust A&E, direct admissions from general practitioners and urgent transfers from DGHs.

We provide 24-hour stroke thrombolysis and a weekday working hours thrombectomy service. Overnight thrombolysis is supervised through a regional ‘Telemedicine’ system. A 2-week survey in July 2017 showed that only 59% patients, who were referred with suspected stroke, had stroke/TIA. Neurological conditions, such as migraine, seizure, syncope, acute vestibulopathy, Bell’s palsy and medically unexplained symptoms were common ‘stroke mimics’. 46% of patients with ‘stroke mimic’ were discharged on the day of admission. Average length of stay was 3 days. A separate survey of acute neurology referrals showed that 58% of patients did not require admission and were managed through an ambulatory care pathway. Patient satisfaction regarding their rapid assessment and diagnosis was high.

Co-location of ANU and HASU allows rapid and effective management of “stroke mimics”.

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**Parallel session 5: Improving treatment, 14.57**

A new UK reproductive care pathway for women with serious mtDNA disease
In March 2015, the UK government passed into law, an amendment to the Human Fertilisation and Embryology Act 1990 to permit ‘Mitochondrial Donation’. This provided a unique legal framework for techniques that make it possible to ‘replace’ mutated mitochondrial DNA (mtDNA) in human oocytes or zygotes. As a group, primary mtDNA diseases are the most prevalent of the inherited neurometabolic disorders, affecting up to 1 in 5000 live births and can often have devastating clinical consequences. To date, treatments focus on palliation of symptoms, while the emergence of reproductive techniques, such as Mitochondrial Donation, offers the first real opportunity to prevent the maternal transmission of some serious forms of mtDNA disease. The Human Fertilization and Embryo Authority (HFEA), the statutory regulatory authority charged with regulating human embryo research in the UK, has devised, a detailed regulatory process for Mitochondrial Donation. To ensure compliance with the HFEA regulations we describe how we have established a high quality, integrated care pathway that provides care that is available to anyone in the UK, and comprehensively involves pathways for couples seeking reproductive advice, IVF pathway for potential mothers with pathogenic mtDNA mutations, a pathway for donors and long-term follow up of children born.

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Parallel session 6: MS & other immune disorders, 14.45

Challenges in reducing hospital deaths in multiple sclerosis

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Introduction: Fifty-five percent of people with multiple sclerosis (pwMS) will die in hospital, above the national average. This study aimed to determine factors that impact place of death for pwMS.

Methods: Retrospective sequential notes review from the UK MS Tissue Bank.

Results: Thirty notes were reviewed from 18/06/12 to 08/09/16. 53% died in hospital, 23% in nursing homes, 13% at home and 10% in hospices. Health interventions increased in year of death versus year prior to death in community (p=0.0369) and primary care (p=0.002) but not in secondary care but were not associated with a non-hospital death (NHD). Recognition of dying (73%, p=0.0024) and having an advanced care plan (ACP) (67%, p=0.0003) were associated with NHD. Family involvement was associated with recognition of dying (p=0.0146) but not with NHD. Multivariable analysis found recognition a person is dying and having an ACP were independently predictive of NHD (R²=0.52, p=0.034). The mean time prior to death of having an ACP (9.6±8.1months) was months prior from when dying was recognised (17.4±27 days, p=0.0004).

Conclusion: Having an ACP and recognition a pwMS is dying are key factors to achieving a NHD. This study highlights the challenges to reducing hospital deaths in MS.

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**Parallel session 6: MS & other immune disorders, 14.57**

MRI abnormalities in MOG antibody disease

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Aims: To analyse the MRI abnormalities of myelin oligodendrocyte glycoprotein-antibody (MOG-Ab) associated demyelinating disease.

Methods: Clinical records and 165 MRIs from 56 patients with MOG-Abs were reviewed.

Results: The median age was 29(18-71) years and 52% percent were female. Common phenotypes included isolated optic neuritis (ON)=17, or transverse myelitis (TM)=16, ON+TM=12, and combinations of above groups with cerebral and/or brainstem involvement=11. Seventeen patients (30%) fulfilled NMOSD 2015 diagnostic criteria.

All patients had brain imaging and 89%(50/56) had spinal imaging. Common areas of MRI brain abnormality involved brainstem(32%), hemispheric white matter(29%), corticospinal tracts(21%), and U-fibres(20%). Dawson's fingers were not detected in any patients.

Cord imaging showed longitudinally extensive myelitis in 69%(20/29) and atrophy in 4%(2/47). Optic nerve imaging was abnormal in 69%(18/26) of patients, with bilateral lesions in 33% and long lesions (orbital and/or canalicular) in 83%.

On serial MRI, radiological improvement was observed in 76%(22/29; median interval- 14 months) and importantly asymptomatic new lesions were absent in 13 untreated patients after a median of 16.5 months.

Conclusions: Apart from optic nerve and spinal cord changes, brainstem and hemispheric white matter abnormalities are common in MOG-antibody disease. Irrespective of treatment, asymptomatic accrual of brain and/or spinal lesions is uncommon.

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**Parallel session 5: Improving treatment, 15.09**

CSF chitinases as novel biomarkers for MND

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The development of biomarkers for amyotrophic lateral sclerosis (ALS, the commonest phenotype of MND) is a priority to reduce diagnostic delay, allow earlier assessment of therapeutic activity, and provide pathogenic insight.

Liquid chromatography tandem mass spectrometry with label-free quantification was used to quantify CSF proteins in individual participant samples. A longitudinal cohort comprised patients with ALS (n=43) and primary lateral sclerosis (PLS, n=6). A cross-sectional cohort comprised healthy (n=20) and disease control patient CSF samples (Parkinson’s disease n=20, MND mimic disorders n=12).
Among 773 identified proteins, significantly elevated levels of three macrophage-derived chitinase proteins were detected in the ALS group, specifically chitotriosidase (CHIT1), chitinase-3-like protein 1 (CHI3L1) and chitinase-3-like protein 2 (CHI3L2). Levels correlated with rate of disease progression (CHIT1 r=0.56, p<0.001; CHI3L1 r=0.31, p=0.028; CHI3L2 r=0.29, p=0.044), and levels of the axonal degeneration marker phosphorylated neurofilament heavy chain (r=0.62, p<0.001; r=0.49, p<0.001; r=0.41, p<0.001). Levels of CHI3L1, but not CHIT1 or CHI3L2, increased over time in those with low initial values (gradient=0.005 log abundance units/month, p=0.001).

Microglial activation has been implicated in the pathogenesis of MND and neuroinflammatory pathways are a major target of therapeutic interest. CSF chitinases may be potential pharmacodynamic as well as diagnostic biomarkers.

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Parallel session 5: Improving treatment, 15.33
St George’s hyperacute neurology: right person, right time

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The St George’s Hospital Hyperacute Neurology Service is a comprehensive consultant-delivered service in a regional neuroscience centre setting that builds on existing recommendations, incorporating hyperacute stroke assessments and the delirium multidisciplinary team. There is proactive daily inreach into acute medicine and the emergency department with Rapid Access Neurology “Hot” clinics providing a means of avoiding admission referrals from primary care and supporting rapid discharge of ambulatory patients from ED. We present data from the first year of this service.

Results: 1299 patients were reviewed (stroke:603; acute neurology:452; Hot clinics:244).

30% of all referrals were discharged directly from the ED and, with “hot” clinics, contributed to 361 admissions avoided.

Stroke mimic utilisation of acute beds (11% reduction) and median thrombolysis times also improved (38v30mins). For admitted acute neurology patients, median(IQR) LoS = 2.0 (0.0-7.0), representing a 50% improvement on previous performance (p<0.001). For hot clinics, the median wait for an appointment= 4.0 days(IQR:2.0-6.0). No diagnostics were required in 25% of cases.

Conclusion: This new service complements existing hyperacute stroke pathways, improving outcomes for all neurology patients presenting to primary care, emergency and acute medical services. In particular, rapid access clinics appear to be an efficient means of providing unscheduled OP care.

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Parallel session 5: Improving treatment, 15.45
Mapping patient pathways for acute functional neurological symptoms

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Introduction: Patients with Functional Neurological Symptoms (FNS) can present acutely, but many hospitals lack specific pathways or services for them. Outpatient FNS cohorts have been studied, but there is little data regarding acute FNS to inform service improvement.

Method: Over an 8 month period at Leeds Teaching Hospitals NHS Trust (UK), the on-call neurology and stroke teams were telephoned regularly. Acute referrals with possible FNS were recorded. Electronic documentation was searched for the following events: symptoms, first presentation, diagnosis, A&E, outpatient clinic, inpatient admission, investigation, and psychological / psychiatric referral. This data was analysed with process mapping software (Fluxicon disco).

Results: We present a dynamic care pathway map using real data, showing 205 patients with possible FNS moving through hospital services over time. Our map visualises the temporal relationships between healthcare utilisation, first presentation, diagnosis and therapy. The picture shows high healthcare burden, with incomplete and slow movement towards appropriate therapy (e.g. clear diagnosis documented in only 66%; referral to psychological therapy in 26%).

Conclusion: Patients with FNS are regularly referred to acute neurological services in Leeds. Our dynamic map shows a high healthcare burden, and slow or incomplete movement to appropriate care, which suggests potential targets for service improvement.

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Parallel session 6: MS & other immune disorders, 15.45
Autoimmune autonomic ganglionopathy: the NHNN experience

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Background: Autoimmune Autonomic Ganglionopathy (AAG) is a rare, immune-mediated condition characterised by subacute pandysautonomia. 50% have auto-antibodies to the ganglionic nicotinic acetylcholine receptor (gAChR), affecting synaptic transmission at autonomic ganglia.

Methods: We describe 13 patients (5 female, median age 47) presenting with widespread autonomic failure, confirmed on cardiovascular, sudomotor and pupillometry testing at the National Hospital for Neurology and Neurosurgery (NHNN), and high gAChR antibody levels (>200pm) measured by radioimmunoprecipitation assay at Oxford University.

Results: Of the 13 patients, 8 had other autoimmune conditions, 3 had antecedent infection and 3 were paraneoplastic. All had orthostatic hypotension, gastro-intestinal and urinary symptoms, 11 had documented pupillary abnormalities (9 mixed sympathetic and parasympathetic deficits, 2 subclinical sympathetic deficits), 11 had secretomotor
dysfunction, 8 had generalised/partial anhidrosis, 8 had sexual dysfunction and 7 had evidence of small fibre dysfunction on neurophysiology.

Ten received immunomodulatory treatment; 6 plasma exchange and 4 combination treatment including intravenous immunoglobulin, mycophenolate and rituximab. Earlier treatment was associated with greater clinical response.

Discussion: Patients with AAG and high gAChR antibody levels have widespread dysfunction of the autonomic nervous system, which can respond dramatically to immunomodulation. Further research is needed to develop robust clinical biomarkers to guide treatment and monitor response.

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Parallel Session 3: Neurodegeneration, 16.15

Neurofilament light protein as a biomarker for Huntington’s disease

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Background: Neurofilament light protein (NfL), a component of the axonal cytoskeleton, has been shown to be increased in cerebrospinal fluid (CSF) and blood and to respond to successful treatment in several neurological diseases. We set out to investigate NfL as a potential biomarker for Huntington’s disease (HD).

Methods: We studied NfL in plasma from 298 participants, in plasma and CSF in 37 participants, and in the R6/2 HD mouse model.

Results: NfL concentration was increased in plasma at every stage of HD including premanifest mutation carriers, rose with progression and had a striking relationship with HTT CAG repeat length. In premanifest HD, baseline plasma NfL predicted subsequent motor onset even after adjustment for age and CAG repeat length. NfL predicted clinical, cognitive and neuroimaging progression, and CSF and plasma levels were strongly associated (Byrne et al, Lancet Neurology 2017). VBM analysis revealed that NfL level predicted atrophy throughout the white matter and in the occipital grey matter (Johnson et al, Neurology 2018). In the R6/2 mouse model, NfL was increased in plasma and CSF and associated with brain volume and clinical measures (Soylu Kucharz et al, Scientific Reports 2017).

Conclusions: NfL is a promising clinical and translational biomarker for HD.

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Parallel session 4: Long term conditions, 16.27

Clinical outcome in MOG-antibody disease: a large single site cohort
First and second author equally contributed to the study

Background: MOG-antibody disease has been recently recognized as a demyelinating condition distinct from Multiple Sclerosis. Methods: A single-site study of 106 MOG-antibody positive patients (including a 63-patient incident cohort) describing the clinical phenotype and outcome.

Results: ON was the most common onset presentation (51%) and was bilateral in about half. From the survival curve analysis in the incident cohort we estimated that 38% of patients relapsed within 18 months. The risk was lower in patients immunosuppressed for >3 months (p= 0.013). Permanent motor disability (EDSS≥6; limited walking distance) and visual acuity ≤6/36 in at least one eye occurred in 3.7% and 13.2% respectively after a median disease duration of 68 months (range 2-484). Permanent bladder dysfunction was present in 23.6% patients and around 2/3 of these had bowel dysfunction. 20% of males had permanent erectile dysfunction (44% of males with TM at onset).

Conclusion: This is the largest single-centre cohort and the only incident cohort published, and shows that MOG-antibody disease is often relapsing but may be modified with 6-12 months of prednisolone. The prognosis is typically good, better than AQP4-antibody positive disease, but many patients are left with significant sphincter and erectile dysfunction and some with visual impairment.

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Parallel Session 3: Neurodegeneration, 16.39
Longitudinal measurement of serum NfL in early familial AD

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A blood-based biomarker able to track early neurodegeneration in Alzheimer’s disease would be valuable. Serum neurofilament-light (NfL) is elevated in familial Alzheimer’s disease (FAD) mutation carriers prior to symptom onset, but exactly how early NfL becomes abnormal and whether it can track change within individuals is uncertain.

We recruited 18 symptomatic carriers of autosomal dominant FAD mutations, 19 presymptomatic carriers, and 11 non-carriers. Blood was taken at baseline, and 26 participants also gave at least one follow-up sample (mean interval = 2.5 years). Serum NfL was measured on the SIMOA platform. A longitudinal mixed effects framework was used to model change in NfL over time.

Serum NfL was increased (p<0.05) in mutation carriers compared with non-carriers 11 years before the estimated time of symptom onset, with rate of change in NfL becoming significantly different 12 years before. However, there was high variability in the inter-individual rate of change in NfL between participants.
Serum NfL concentration, and its rate of change, are sensitive, at the group level at least, to very early AD-neurodegeneration. However, the high variability between individuals in NfL rate of change may make it difficult at present to use this measure to track early change in individual patients.

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**Parallel Session 3: Neurodegeneration, 16.51**

Genetic associations of ICD in Parkinson’s disease

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Introduction: Impulse Control Disorders (ICD) are a potentially devastating side-effect of dopaminergic therapy in Parkinson’s disease (PD). We explore the genetic factors associated with ICD in Tracking Parkinson’s/PRoBaND – a UK-wide cohort of early-stage PD.

Methods: Participants were diagnosed with PD within 3 years and had longitudinal assessment including the Questionnaire for ICD in Parkinson’s (QUIP) for up to 5 years. We defined cases as having any positive response to the QUIP (lax criteria) or 2 positive responses in any domain (strict criteria). We performed a candidate-gene analysis based on systematic review, followed by a genome-wide association study. We used age at onset, gender, and three significant principle components as covariates.

Results: After clinical and genetic quality control steps, we analysed 1602 participants. Prevalence was significantly affected by classification criteria (strict/lax): ICD – 26.8%/11.1%, IRB 29.3%/27.2%, any 31.7%/41.9%. Six SNPs in dopamine, glutamate and adreno- receptor genes achieved nominal significance (p<0.05) in the candidate study. We have identified several SNPs in the GWAS that approach genome wide significance (p<5x10⁻⁷).

Conclusions: This work is the first genome-wide study of genetic determinants of ICD. Our findings support the hypothesis of genetic determinants of ICD in Parkinson’s and further work will allow understanding of the biology of ICD.

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