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ADVANCES IN CLINICAL NEUROSCIENCE & REHABILITATION

In this issue

Royal College of General Practitioners
THAMES VALLEY FACULTY

PRIMARY CARE NEUROLOGY SOCIETY P-CNS

Neurology Red Flags: What to do next?
Saturday 14 October 2017, 09:30—13:00
PJ Care, 153 Sherwood Drive, Bletchley, MK3 6RT

Fees: RCGP Member: £45.00, Non Member: £60.00

Book online today at :
http://www.rcgp.org.uk/learning/london-and-south-england/thames-valley-faculty/neurology-red-flags.aspx

Speaker
Dr Martin Turner is a consultant neurologist at Oxford University's Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, where he is a senior researcher in motor neurone disease. He is a regular lecturer to the regional GP VTS on how to approach neurological symptoms.

About the workshop
This morning workshop is an ideal opportunity for primary care professionals refresh their knowledge and skills in identifying and taking appropriate action when patients present with key neurology 'red flags' symptoms.
The workshop is divided in to a number of sessions, each tackling a different symptom (e.g. headache, weakness, tingling, dizziness incl. LOC, tremor, memory). There will be ample opportunity for you to discuss issues currently challenging you.

If you have any cases you may be managing in your practice and you would like to discuss these, to ensure Dr Turner has an opportunity to review the case prior to the workshop, please email a brief summary info@p-cns.org.uk. We recommend that you anonymise the case detail.

Outline programme:

09.00 – Registration
09.30 – Welcome and Introduction
09.40 – General principles: onset and stereotypy
09.50 – Headaches
10.30 – Loss of Consciousness
10.50 - Dizziness/unsteadiness
11.10 – Q and A Session
11.25 – Coffee/Tea
11.45 – Tingling/weakness
12.10 – Cognitive problems
12.40 – Q&A / tricky cases from GPs

Please note that lunch is not provided but there will be tea/coffee at registration and in the morning break. A certificate of attendance will also be provided.

P-CNS
The registration fee of £45 includes free membership of the Primary Care Neurology Society – which normally costs £45. This will give you access to ebrain - details available from our website, www.p-cns.org.uk
Complete the online modules and collect CPD points!

Why choose RCGP?	Notes
The RCGP is the professional membership body for General Practitioners in the UK and overseas. We are committed to improving patient care, clinical standards and GP training.	The venue is PJ Care, 153 Sherwood Drive, Bletchley, Milton Keynes MK3 6RT Refreshments included. There is ample free parking.

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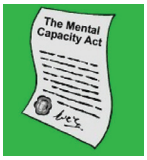
community therapists network

Mental Capacity Assessment – Getting it right!
22nd September 2017, Manchester



Lead by two leading experts in the field, Mark Jayes, a speech and language therapist since 2003, with specialist knowledge of Mental Capacity Assessment and Mathieu Culverhouse, Associate at Irwin Mitchell with expertise in Mental Capacity Law, this practical workshop will help you get to grips with assessment of mental capacity, including an overview of common communication disorders and how these can impact on mental capacity.

To learn more and secure one of 5 special offer places at £90 please use the code ACNR90 when registering online, via www.communitytherapy.org.uk

Learning How to Use the TOM
5th October 2017, London

This workshop, lead by Prof Pam Enderby, will enable participants to be able to use the Therapy Outcome Measure in their clinical practice, with confidence. Delegates will go away with a greater understanding of how best to collect and measure outcomes data on clients receiving treatments. The day includes both theoretical and practical components, with ample opportunity to practice with the TOM and rate various patients, with guidance from Prof Pam Enderby.

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Cover images

Our front cover images are taken from the exhibition Andrew Marr: Strokes of Colour at Corke Art Gallery, Liverpool, UK.

This is Andrew Marr's first public exhibition, made up of paintings created since his stroke in 2013. It tells two stories, of recovery and natural progression.

All profits from the exhibition are going to ARNI (Action Rehabilitation for Neurological Injuries). Exhibition catalogues are still available (£5) as are a number of paintings. See www.artinliverpool.com/featured-artist-andrew-marr-strokes-colour-corke-art-gallery/

The picture below was a gift to Tom Balchin, Director of ARNI, by Andrew Marr at the end of his first year of rehabilitation. The picture was painted before his stroke.

Michael Zandi Co-Editor.

The impact of spinal disease on life is huge. Rosie Tween writes a personal perspective on her own spinal stroke, and highlights the work of the charity the Back Up Trust – backuptrust.org.uk, and how she and a team climbed Mount Snowden in July this year raising funds for the charity. Jason Yuen and Peter Whitfield from Plymouth provide a 60 year long view of surgery for degenerative cervical spine disorders, where patient selection but also the choice of technique are crucial. This is a helpful account for the general clinic to aid patient selection and help inform patients of what they may face.

A common clinical problem in the clinic is of visual loss due to optic neuritis. The old optic neuritis treatment trials have led many to be conservative in the treatment of this entity. But as we learn more of important mimics of Multiple Sclerosis related optic neuritis, e.g. aquaporin 4 antibody related optic neuritis, it is clear that empirical therapy with steroids and plasma exchange while carrying out further investigations, in selected individuals, may be justified. Clinical assessment is not fully reliable to help us distinguish the differential diagnoses – Multiple Sclerosis, from AQ4 or myelin oligodendrocyte glycoprotein (MOG) antibody disease, sarcoid, tuberculosis, HIV and other infectious causes, post-infectious, lymphomatous, carcinomatous and other causes. Imaging and same day point of care antibody testing and CSF analysis techniques to help us are not yet available.

Simon Broadley, Elham Khalili, Saman Heshmat and Laura Clarke from the Gold Coast write a comprehensive update on neuromyelitis optica, aquaporin 4 (AQ4) antibody and MOG antibody related disease for 2017. This can be a devastating disorder, with a clear message that early diagnosis is needed and aggressive treatment is justified. There remains uncertainty in the best standard of care of immunosuppression long term, with a need for clinical trials but with the help of biomarker development to help us assess disease mechanisms and changes in real time.

JMS Pearce in our historical article on optic neuritis takes us away from 2017, first to 9th century Arabic texts, then to familiar names Buzzard, Allbutt, and Devic, and showcases the contributions of Edward Nettleship (1845-1913) to the study of optic neuritis.

We hope you enjoy this issue which includes book and conference reviews, an ABN trainee article on the MRCP neurology exam by Ann Donnelly, and a case report.

Mike Zandi, Co-Editor
Email. Rachael@acnr.co.uk

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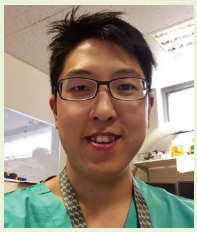
Anterior cervical discectomy and fusion (ACDF) for degenerative cervical diseases – Six decades on



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Abstract
Anterior cervical discectomy and fusion (ACDF) has been used to treat degenerative cervical spine diseases for almost six decades. In this literature review, we have summarised the history, indications, outcome and complications of the procedure. We also provide technical details on surgery. Despite the emerging new technical advances such as cervical arthroplasty, evidence continues to support the use of ACDF, given its well-established safety profile and effectiveness.

Introduction

Anterior cervical discectomy and fusion (ACDF) has been one of the most commonly performed procedures for degenerative spinal diseases, with more than five million operations conducted in the United States between 1990 and 1999.[1] The main indications are for the treatment of cervical myelopathy and radiculopathy secondary to cervical disc prolapse and osteophyte compression. It has also been used to treat a range of other cervical diseases (mainly between C3 and T1 vertebrae) related to cervical instability (degenerative, traumatic, oncological, infectious, inflammatory, iatrogenic).[2]

History of the procedure

Prior to 1950, cervical spine surgery was primarily performed via a posterior approach.[3] The anterior cervical approach was initially described in the 1950s to access the oesophagus.[4] In 1958, Smith and Robinson[5] applied the approach to cervical discectomy and interbody fusion using a horseshoe-shaped graft, harvested from the iliac crest in 14 patients suffering radiculopathy. Degenerative changes had been demonstrated by myelography and discography. In this approach, the disc was removed and the space was filled by bone graft to achieve fusion. Posterior osteophytes were not removed and the posterior longitudinal ligament (PLL) was left intact. This indirectly decompressed the nerve root by distraction. Nine patients had an excellent outcome and four had good or fair results. In the same year, Cloward[3] independently reported interbody arthrodesis using dowel-type graft harvested from the iliac crest. In addition, Cloward's approach also removed osteophytes, leaving the PLL intact. The majority of the 47 cases (all of which had neck, shoulder and/or upper arm pain) reported complete relief. Other types of grafting e.g. the onlay graft developed by Bailey and Badgley[6] and the keystone graft developed by Simmons and Bhalla[7] have not been widely adopted.

Diagnosis

Neck and shoulder pain is a common complaint in primary care, hence careful selection is required to identify patients with pathology that warrants ACDF. The age-adjusted incidence of cervical radiculopathy is 83 per 100,000 persons (less common than lumbar radiculopathy), with potential risk factors including female gender, white race, cigarette smoking, axial load bearing, and prior lumbar radiculopathy.[8]

A recent literature review[9] found no high-quality study that had measured the incidence or prevalence of cervical spondylotic myelopathy but the prevalence of surgically treated cervical spondylotic myelopathy was estimated as 1.6 per 100,000 persons.

Radiculopathy

As each nerve root exits above the pedicle of its like-numbered vertebra, a herniated disc usually impinges on the nerve root exiting from the neural foramen at the level of herniation (e.g. C4/C5 disc herniation tends to affect root C5). A summary of cervical disc syndromes is given in Figure 1.[10] Root

Figure 1: Cervical disc syndromes. Adopted from [10].

Level	C4/5	C5/6	C6/7	C7/T1
Percentage of cervical discs/%	2	19	69	10
Compressed root	C5	C6	C7	C8
Reflex diminished	Deltoid and pectoralis	Biceps and brachioradialis	Triceps	Finger jerk (exaggerated)
Motor weakness	Abduction > 90 degrees; elbow flexion	Forearm flexion	Forearm extension	Hand intrinsics
Paraesthesia	Shoulder	Upper arm, thumb and radial forearm	Fingers 2 and 3, all fingertips	Fingers 4 and 5

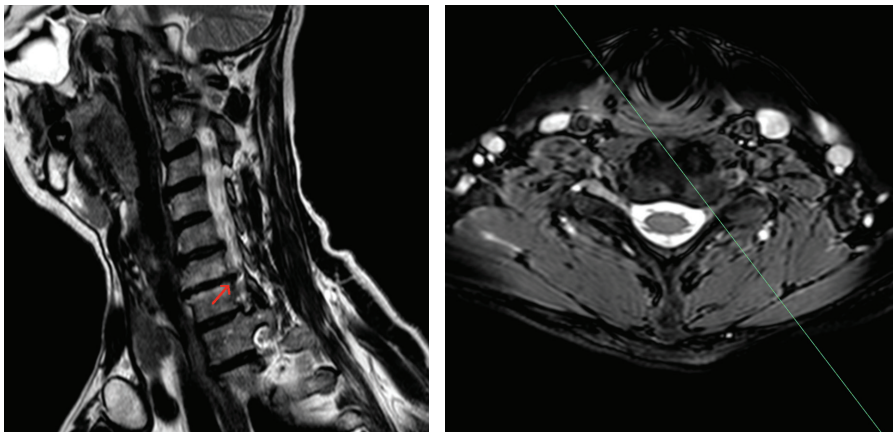


Figure 2: An example of MRI imaging in cervical disc herniation (C6/C7).
a) (left image) Parasagittal view, with the axis of the slice at 90 degrees to the axis of the exiting nerve root. Arrow denotes herniated disc at level of interest. b) (right image) Axial view.

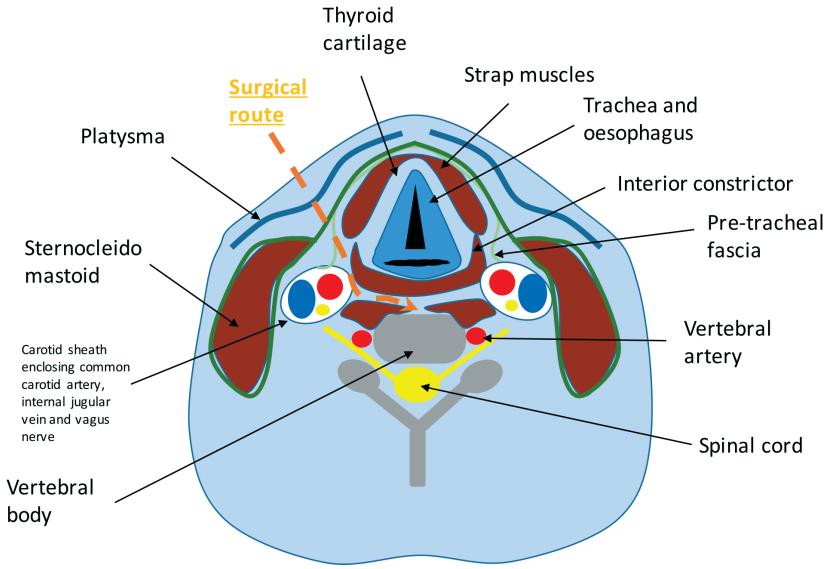
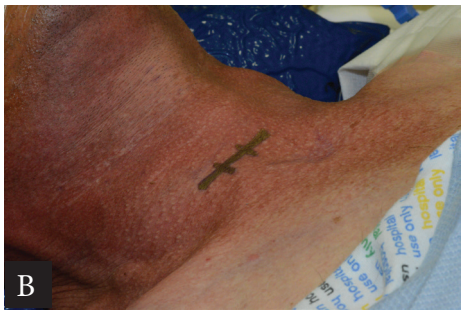
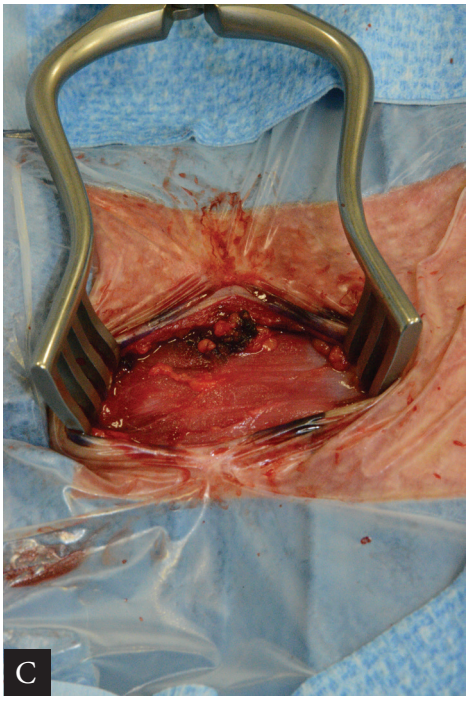
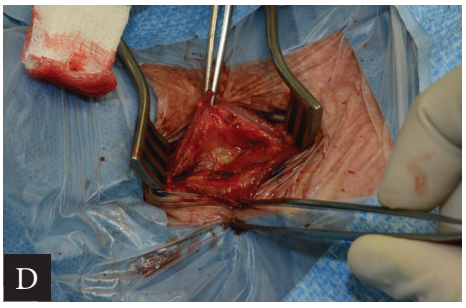
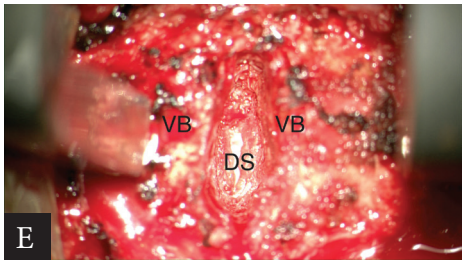


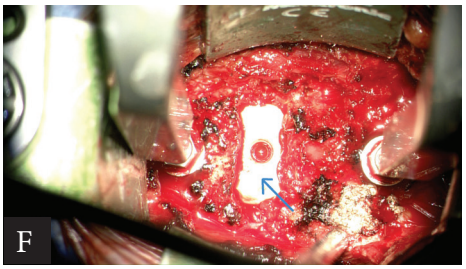
Figure 3: Surgical approach in an ACDF.
A) (Above) Simplified scheme of cross-section of the neck with the arrow denoting the path of approach. For more detailed anatomy, please consult anatomy textbooks such as [64].
B) Example of incision at C6/C7 level.
C) Skin incision down to platysma.
D) Opening of platysma showing anterior border of sternocleidomastoid muscle.
E) Post-removal of disc material by electric drills and curette. VB, vertebral body; DS, disc space.
F) PEEK spacer in-situ (arrow).











compression usually causes dermatomal or myotomal pain, paraesthesia or numbness and a range of lower motor neuron (LMN) signs including muscle atrophy, fasciculations, weakness in a specified myotome, reduced reflexes, as well as sensory changes in a dermatomal distribution.

A few clinical tests have been described to aid diagnosis. Axial loading of the head while tilting the head towards the symptomatic side may reproduce the radicular symptoms (Spurling's sign); whereas axial traction may alleviate them. Symptoms may also be relieved by shoulder abduction in a sitting patient. These clinical tests tend to be highly specific but not very sensitive.[11]

Myelopathy

Myelopathy may be acute or chronic; complete or incomplete. There may or may not be a history of acute trauma. Degenerative cervical myelopathy (DCM), defined as symptomatic myelopathy associated with degenerative arthropathic changes in the spine axis is a leading cause of acquired spinal cord compromise.[12] Commonly there are signs of upper motor neuron (UMN) compromise – weakness with spasticity, as well as brisk reflexes and ankle clonus. In addition, loss of sensation below level of involvement and autonomic dysfunction may be evident. Other signs include Lhermitte's sign (an electric shock-like sensation in the neck on flexion of the neck), a positive Hoffmann's reflex, Babinski's sign and scissoring gait in some patients. Central cord syndrome is associated with certain types of injuries such as neck hyperextension, often in a patient with pre-existing osteophytes encroaching upon the spinal canal.

Diagnosis is usually supported by the use of magnetic resonance imaging (MRI) unless

contraindicated. In addition to sagittal and axial views, parasagittal oblique views can be used to visualise neural foramina perpendicular to the plane of root exit (Figure 2). This enhances the sensitivity of MRI for the detection of small disc prolapses encroaching upon the exiting nerve root. If MRI is contra-indicated, computed tomography (CT) and/or CT myelogram are used. Electrophysiological studies are performed only when there is diagnostic uncertainty.

An early study in 1963[13] followed 51 patients with cervical radiculopathy over two to 19 years. In this cohort, no patient with radicular pain progressed to have myelopathy. In a survey[14] of over 500 radiculopathic patients with a median duration of follow-up of 4.9 years, recurrence of the condition occurred in 31.7%, and 26% underwent surgery for cervical radiculopathy. Radicular pain and focal neurology were predictors for operation. In a cohort study of 26 consecutive patients with radiculopathy followed up over 1 year, over 90% of patients improved without surgery;[15] operative management is therefore reserved for patients with intractable pain or progressive neurology.[16] In the case of myelopathy, there are no large randomised trials on which to base treatment recommendations but for patients with more severe myelopathy, progressing deficits or acute deterioration, surgical decompression is recommended.[17-19] Surgery to prevent neurological injury in patients with asymptomatic cervical spondylotic disease is not recommended as risk of minor trauma causing deterioration is very low.[20]

Operative Technique

The technique used for ACDF varies widely among surgeons. We outline our routine technique.

Positioning

The patient is positioned supine with a vacuum horseshoe-shaped sandbag placed in the nape of the neck, supporting the head bilaterally. Position is neutral, and horizontal. Slight head-up, or even head-down tilt may be used to facilitate visualisation of a specific disc space.

Skin incisions and platysma division

A 4cm transverse skin crease incision is made at the appropriate level. Anatomical landmarks are used to identify the correct level e.g. thyroid cartilage at the level of C4 and cricoid cartilage at C6. Pre-incision fluoroscopy is used by some surgeons to confirm the level of the approach. The skin incision extends medially from the anterior border of right sternocleidomastoid muscle (SCM) (mainly for the ease of right-handed surgeon). The platysma is exposed and then divided along the direction of the muscle fibres (although some prefer dividing the platysma transversely).

Surgical plane and discectomy

The anterior triangle is then dissected, developing a plane between carotid sheath laterally and the larynx and oesophagus medially, as shown in Figure 3. The carotid pulse should be confidently identified using a gloved finger inside the wound. The midline structures are retracted en bloc to avoid retraction on the recurrent laryngeal nerve (RLN). An avascular plane is dissected down to the longus colli muscles, which are then undercut bilaterally using diathermy and a periosteal elevator. Toothed self-retaining retractors are inserted under the longus colli fibres to provide a clear surgical view. Fluoroscopy is always used at this stage to confirm the operating level. Any anterior osteophytes may be removed using electrical drill or Kerrison punch. Caspar pins are used to distract adjacent levels. Discectomy is performed using a size 15 scalpel, straight microrongeurs and microcurettes under the operating microscope. Posterior osteophytes and the posterior aspect of the uncus are removed with the high speed drill, currettes and micro upcuts. The senior author recommends use of a match-head drill to perform this manoeuvre. The posterior longitudinal ligament (PLL) is carefully opened, away from the site of maximal neural compression. This is facilitated with a size 10 Rhoton hook and an upcurved Karlin blade. The ligament is resected using a 1mm upcut to enable good visualisation of the dura and the nerve root origins. A 2mm upcut is sometimes used at this stage. A 16 Rhoton hook is useful to probe the exiting foramen.

Graft

A PEEK cage packed with bone chips/dust obtained from removal of osteophytes is widely used as graft material for interbody fusion. The cage may be straight or incorporate a 5 degree angulation to correct kyphotic deformity. A number of grafts have been used to promote fusion. Autologous bone grafts are preferred to promote osteogenesis, osteoinduction and osteoconduction;[21] these are usually acquired locally from osteophytes. In order to reduce donor site (traditionally iliac crest, fibula or rib) morbidities,[22] such as pain, infection and haematoma, a number of substitutes such as allogenic bone graft and synthetics have been developed. There are also other options including ceramics[23] and more controversially, bone morphogenic proteins (BMP).[24] In addition, cages are generally made of plastics e.g. polyetheretherketone (PEEK)[25] or metal e.g. titanium.[26] Carbon fibre cages[27] have also shown promising fusion rates.

Plate vs. no plate

There is currently no consensus in the option of anterior plates in ACDF. Our centre does not routinely use anterior cervical plates when performing a 1 or 2 level ACDF. A recent randomised trial[28] indicated that multiple-level fusions may have better clinical outcome when a dynamic plate design is used but the use of a plate in single-level ACDF remains controversial. Plating in anterior cervical operation was initially developed for cervical spinal trauma such as fractures and dislocations.[21] For the treatment of cervical spondylosis, it may confer the theoretical benefit of additional stability, maintenance of cervical lordosis and prevention of extrusion of bone graft material. A number of plating and fixation device designs[29] have been developed – dynamic plate, locking screws to promote stability and alignment, and to reduce risk of visceral damages. A zero-profile system fixing the cage onto vertebral body with screws has shown comparable clinical outcomes and fusion rates relative to using anterior cervical plating, and is reported to have reduced risk of dysphagia or degenerative change of adjacent segment.[21] More recently, bioabsorbable plates appear to achieve fusion rate and outcome comparable to the results associated with metallic plates.[30]

Post-operative Care

Post-operatively, it is imperative to monitor the patient's airway and neurological function with clear documentation. A rapidly developing wound haematoma can threaten airway patency and may require immediate evacuation. Any impairment of neurological function warrants an MRI scan to assess the cause and guide treatment options. Some surgeons request a post-operative cervical X-ray to confirm operative level, cage position and the position of any plating system (Figure 4). This rarely changes clinical management and is of doubtful clinical value.

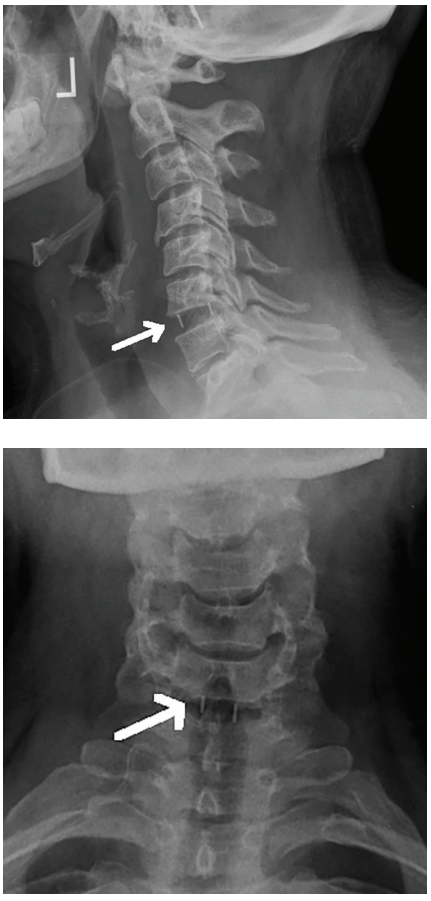


Figure 4: An example of post-operative cervical radiograph after an ACDF.
a) (top image) Lateral.
b) (bottom image) Antero-posterior.
The white arrows denote position of the graft.

Measured outcomes

With cervical myelopathy, 50 to 80% of patients are reported to improve after surgery, while 5 to 30% continue to report ongoing or progressive symptoms.[31-33] Positive prognostic factors in improving the patient-identified clinical outcome (as defined by modified Japanese Orthopedic Association scale) were younger age, shorter duration of symptoms, non-smoking status, and lack of significant gait impairment.[34]

Factors reported to predict a poor response to surgery include older age, intramedullary signal abnormality on MRI, especially if multi-segmental and with abnormalities on T1 as well as T2-weighted images, more severe preoperative disability, longer duration of symptoms preoperatively, narrow preoperative canal size and multisegmental compression.[17]

The surgical outcome for cervical radiculopathy is more equivocal. Randomised controlled trials showed that it provides short term benefit in terms of pain and neurological deficit relative to conservative treatment but by one to two years, there was no significant difference in outcome.[35,36] Therefore conservative management was recommended by the authors as the initial modality of treatment.

Alternative treatments

Non-surgical options generally involve pain management and physiotherapy. Of note, a 10-year prospective randomised study[37] involving 64 patients showed no significant benefit with surgical treatment for mild to moderate cervical myelopathy. Neuroprotective treatments such as riluzole, a sodium-glutamate antagonist are also being trialled at the moment.[38]

The main anterior surgical alternatives to ACDF in the treatment of degenerative cervical diseases include anterior corpectomy and anterior discectomy without fusion. Posterior decompression (with or without fusion) via a limited exposure and foraminotomy (for root compression), a laminectomy or laminoplasty (for cord compression) remain options, particularly when the compression is posterior.

In terms of surgical treatment, there is no consensus regarding the indications and timing. Also it is not known which type of surgical procedure is best as Class I randomised trials are lacking.[17] The anterior approach has the theoretical benefit of removing any compressive disc material and anterior osteophytes, as well as facilitating fusion of adjacent vertebral bodies directly. Posterior cervical pathology may be better treated with posterior approaches. Minimally invasive posterior decompression has been shown to be as effective as ACDF in selected patients with myelopathy.[39]

The use of an implant to act as a spacer for fusion has become increasingly common, but a prospective, randomised trial[40] suggested that even though the incidence of fusion was indeed higher, patient satisfaction and rate of return to preoperative activity level were similar regardless of an ACD or ACDF. Another trial[41] showed that posterior cervical foraminotomy, ACDF and anterior cervical discectomy without fusion are equally successful in treating cervical radiculopathy caused by a unilateral acute herniated cervical disc.

ACDF vs cervical arthroplasty

The use of an artificial joint instead of fusion to retain mobility at the level of operation has long been proposed. A metal-on-metal, ball-in-socket Cummins-Bristol design reported outcomes in 1998.[42] Not only does it have the potential to provide a better range of movement but it also theoretically reduces motion and pressure at adjacent segment[43] and hence incidence of adjacent segment disease (ASD). Nonetheless, a number of complications such as screw pullout had been reported and surgical removal of the hardware proved to be considerably difficult.[42] A range of new designs and materials have been developed. Examples include the second-generation Bristol design (also known as Prestige®) which replaced the inferior hemispherical cup of the Cummins design with a shallow ellipsoid saucer to allow for more movement, and they have shown promising results in the trials.[23,44] Another design known as the Bryan® disc adopted a metal-on-plastic model and also showed hopeful preliminary results.[44,45]

The literature has however not shown arthroplasty conferring significant long-term advantage: a Cochrane review[46] with 2400 participants showed a small but statistically significant favourable outcome for arthroplasty compared to ACDF but it was withdrawn due to non-compliance with the Cochrane Commercial Sponsorship Policy.[47] Another systemic review[48] suggested no superiority of cervical total disc replacement relative to fusion operation. Another meta-analysis,[49] showed that arthroplasty does not reduce the rate of ASD compared to ACDF. More studies are required to confirm its efficacy and safety.

Complications

Factors associated with increased operative risk have included: increasing age, medical co-morbidity (American Society of Anesthesiology (ASA) class > 2), chronic obstructive pulmonary disease, bleeding disorder, coexisting diabetes mellitus, OPLL and longer operative duration.[50,51] A large retrospective study also suggested that the male gender increased the risk of airway complications.[51]

Complications of ACD (with or without fusion) can be classified as:

1) general complications e.g. anaesthetic risks, infection and haemorrhage;
2) access-related complications e.g. oesophageal, neurovascular and tracheal damage;
3) discectomy- and fusion-related device-related risks e.g. damage to nerve root or spinal cord and loosening of screws;
4) risks of non-union, compressive residual disease and ASD.

A summary of complication rate from various recent studies is shown in Figure 5.[52-57]

There is insufficient evidence to support differences in rates of complications across surgical techniques.[58] A retrospective American study[59] with 36000 patients found an overall complication rate of 15.6% after ACDF, 29.2% after posterior fusion, 41.1% after combined anterior and posterior fusion, and 22.4% after laminoplasty. The author acknowledged that the rates are considerably higher than other similar studies and attributed the discrepancy

Figure 5: Summary of complication rate in recent studies. [52-57]

Key Complications	Complication rate / %	References
Post-op haematoma	0.2 to 5.6	Tew, Fountas, Nanda
RLN palsy	0.05 to 7.1	Robinson, Tew, Flynn, Fountas, Nanda
Dysphagia	0.15 to 9.5	Tew, Fountas, Nanda
Horner's syndrome	0.02 to 3.6	Robinson, Tew, Flynn, Fountas
Pharyngeal or oesophageal perforation	0.1 to 0.3	Tew, Fountas, Nanda
Durotomy	0.5 to 1.3	Fountas, Nanda
Worsening neurology	0.2 to 0.88	Tew, Flynn, Fountas
Wound infection	0.1 to 9.5	Robinson, Fountas, Nanda, Gruskay
Graft extrusion	0 to 0.88	Tew, Fountas, Nanda
Mortality	0 to 0.2	Robinson, Tew, Flynn, Fountas, Nanda, Gruskay
Overall Complication	0.45 to 19.6	Robinson, Tew, Flynn, Fountas

to their accurate data sourced from commercial claims, outpatient services and Medicare databases, reducing the risk of losing follow-up outcomes.

However, different techniques are often associated with different types of complications:[60] for example, 1) dysphagia is more frequent following anterior surgery, 2) wound infection is more common following posterior surgery, and 3) higher rates of axial pain are observed following laminoplasty compared to ACDF.

Dysphagia and dysphonia

Dysphagia and dysphonia are both common complications after ACDF. They are likely to be multifactorial such as secondary to visceral oedema or neuropraxia of RLN or superior laryngeal nerve secondary to retraction. The majority (67 to 100%) of patients with vocal cord palsy recover within 12 months and most recover within 6 to 12 weeks.[61] It is imperative the surgeon is aware of the anatomy (e.g. the RLN is located in the tracheoesophageal recess) during traction. Due to the increased risk of dysphonia from the anterior approach, professional speakers and singers need to be counselled with care.

Equipment-related

With respect to locking plate-related complications, a retrospective study involving 2000 patients[62] estimated a 10.7% complication rate, including loosening or breaking of the plates and screws or malpositions that threatened tracheoesophageal or neurovascular structures. These were radiologically diagnosed and only a small number required re-operation. In addition, plating appears to increase the risk of adjacent level ossification (ALO), the clinical significance of which is debatable.[63]

Conclusions

Six decades after the procedure of ACDF was first used to treat degenerative spine diseases, the literature has supported its position as the mainstay of treatment for a number of cervical spinal pathologies. It is an established, safe and effective procedure, with an acceptable complication profile. A variety of techniques have been adopted and in this article we have outlined the indications and technique we routinely use in our centre. Some issues remain controversial – such as the use of plating and arthroplasty, and require further studies.

REFERENCES

1. Angevine PD, Arons RR, McCormick PC. *National and regional rates and variation of cervical discectomy with and without anterior fusion, 1990-1999.* Spine (Phila Pa 1976) 2003;28(9):931-9; discussion 940.
2. Eck J, Vaccaro A. *Surgical Atlas of Spinal Operations.* 2013: Jaypee Brothers Medical Publishers.
3. Cloward RB. *The anterior approach for removal of ruptured cervical disks.* J Neurosurg, 1958;15(6):602-17.
4. Lahey FH, Warren KW. *Esophageal diverticula.* Surg Gynecol Obstet. 1954;98(1):1-28.
5. Smith GW, Robinson RA. *The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion.* J Bone Joint Surg Am. 1958;40-A(3):607-24.
6. Bailey RW, Badgley CE. *Stabilization of the cervical spine by anterior fusion.* J Bone Joint Surg Am. 1960;42-A:565-94.
7. Simmons EH, Bhalla SK. *Anterior cervical discectomy and fusion. A clinical and biomechanical study with eight-year follow-up.* J Bone Joint Surg Br. 1969;51(2):225-37.
8. Corey DL, Comeau D. *Cervical radiculopathy.* Med Clin North Am. 2014;98(4):791-9, xii.
9. Boogaarts HD, Bartels RH. *Prevalence of cervical spondylotic myelopathy.* Eur Spine J. 2015;24 Suppl 2:139-41.
10. Greenberg MS, Greenberg MS. *Handbook of neurosurgery.* 7th ed. 2010; Tampa, Fla. New York, N.Y.: Thieme Medical Publishers. xiv;1337.
11. Viikari-Juntura, E, Porras M, Laasonen EM. *Validity of clinical tests in the diagnosis of root compression in cervical disc disease.* Spine. (Phila Pa 1976), 1989;14(3):253-7.
12. Kato S, Fehlings M. *Degenerative cervical myelopathy.* Curr Rev Musculoskelet Med. 2016;9(3):263-71.
13. Lees F, Turner JW. *Natural History and Prognosis of Cervical Spondylosis.* Br Med J. 1963;2(5373):1607-10.
14. Radhakrishnan K et al. *Epidemiology of cervical radiculopathy.* A population-based study from Rochester, Minnesota, 1976 through 1990. Brain.1994;117 (Pt 2):325-35.
15. Saal JS, Saal JA, Yurth EF. *Nonoperative management of herniated cervical intervertebral disc with radiculopathy.* Spine (Phila Pa 1976). 1996;21(16):1877-83.
16. Galbraith JG et al. *Operative outcomes for cervical myelopathy and radiculopathy.* Adv Orthop. 2012;2012:919153.
17. Levin K. *Cervical spondylotic myelopathy.* UpToDate 2013 [cited 2016 1/6].
18. McCormick WE, Steinmetz MP, Benzel EC. *Cervical spondylotic myelopathy: make the difficult diagnosis, then refer for surgery.* Cleve Clin J Med, 2003;70(10):899-904.
19. Robinson J, Kothari MJ. *Treatment of cervical radiculopathy.* 2016 [1/6/2016].
20. Bednarik J et al. *Are subjects with spondylotic cervical cord encroachment at increased risk of cervical spinal cord injury after minor trauma?* J Neurol Neurosurg Psychiatry. 2011;82(7):779-81.
21. Song KJ, Choi BY. *Current concepts of anterior cervical discectomy and fusion: a review of literature.* Asian Spine J, 2014;3(4):531-9.
22. Silber JS et al. *Donor site morbidity after anterior iliac crest bone harvest for single-level anterior cervical discectomy and fusion.* Spine (Phila Pa 1976). 2003;28(2):134-9.
23. Suetsuna F et al. *Anterior cervical fusion using porous hydroxyapatite ceramics for cervical disc herniation. a two-year follow-up.* Spine J, 2001;1(5): 348-57.
24. Carragee EJ, Hurwitz EL, Weiner BK. *A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned.* Spine J. 2011;11(6):471-91.
25. Celik SE, Kara A, Celik S. *A comparison of changes over time in cervical foraminal height after tricortical iliac graft or polyetheretherketone cage placement following anterior discectomy.* J Neurosurg Spine. 2007;6(1):10-6.
26. Whitecloud TS. 3rd, *Modern alternatives and techniques for one-level discectomy and fusion.* Clin Orthop Relat Res. 1999;(359):67-76.
27. Marotta N et al. *Five-year outcome of stand-alone fusion using carbon cages in cervical disc arthrosis.* Eur Spine J. 2011;20 Suppl 1:S8-12.
28. Nunley PD et al. *Choice of plate may affect outcomes for single versus multilevel ACDF: results of a prospective randomized single-blind trial.* Spine J. 2009;9(2):121-7.
29. Haid RW et al. *The Cervical Spine Study Group anterior cervical plate nomenclature.* Neurosurg Focus. 2002;12(1):E15.
30. Tomasino A. et al. *Bioabsorbable instrumentation for single-level cervical degenerative disc disease: a radiological and clinical outcome study.* J Neurosurg Spine. 2009;11(5):529-37.
31. Chiles BW 3rd et al. *Cervical spondylotic myelopathy: patterns of neurological deficit and recovery after anterior cervical decompression.* Neurosurgery. 1999;44(4):762-9; discussion 769-70.
32. Ebersold MJ, Pare MC, Quast LM, *Surgical treatment for cervical spondylitic myelopathy.* J Neurosurg. 1995;82(5):745-51.
33. Lunsford LD, Bissonette DJ, Zorub DS. *Anterior surgery for cervical disc disease. Part 2: Treatment of cervical spondylotic myelopathy in 32 cases.* J Neurosurg. 1980;53(1):12-9.
34. Tetreault L et al. *Predicting the minimum clinically important difference in patients undergoing surgery for the treatment of degenerative cervical myelopathy.* Neurosurg Focus. 2016;40(6):E14.
35. Peolsson A. et al. *Physical function outcome in cervical radiculopathy patients after physiotherapy alone compared with anterior surgery followed by physiotherapy: a prospective randomized study with a 2-year follow-up.* Spine (Phila Pa 1976), 2013;38(4):300-7.
36. Persson LC et al. *Cervical radiculopathy: pain, muscle weakness and sensory loss in patients with cervical radiculopathy treated with surgery, physiotherapy or cervical collar. A prospective, controlled study.* Eur Spine J. 1997;6(4):256-66.
37. Kadanka Z et al. *Cervical spondylotic myelopathy: conservative versus surgical treatment after 10 years.* Eur Spine J. 2011;20(9):1533-8.
38. Fehlings MG et al. *Rationale, design and critical end points for the Riluzole in Acute Spinal Cord Injury Study (RISCIS): a randomized, double-blinded, placebo-controlled parallel multicenter trial.* Spinal Cord. 2016;54(1):8-15.
39. Abbas SF et al. *A comparison of minimally invasive posterior cervical decompression and open anterior cervical decompression and instrumented fusion in the surgical management of degenerative cervical myelopathy.* Neurosurg Focus. 2016;40(6):E7.
40. Dowd GC, Wirth FP. *Anterior cervical discectomy: is fusion necessary?* J Neurosurg. 1999;90(1 Suppl):8-12.
41. Wirth FP et al. *Cervical discectomy. A prospective analysis of three operative techniques.* Surg Neurol. 2000;53(4):340-6;discussion 346-8.
42. Cummins BH, Robertson JT, Gill SS. *Surgical experience with an implanted artificial cervical joint.* J Neurosurg. 1998;88(6):943-8.
43. Wigfield C et al. *Influence of an artificial cervical joint compared with fusion on adjacent-level motion in the treatment of degenerative cervical disc disease.* J Neurosurg. 2002;96(1 Suppl):17-21.
44. Mummaneni PV et al. *Cervical artificial disc replacement versus fusion in the cervical spine: a systematic review comparing long-term follow-up results from two FDA trials.* Evid Based Spine Care J. 2012;3(S1):59-66.
45. Goffin J et al. *Intermediate follow-up after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis: single-level and bi-level.* Spine (Phila Pa 1976), 2003;28(24):2673-8.
46. Boselie TF et al. *Arthroplasty versus fusion in single-level cervical degenerative disc disease: a Cochrane review.* Spine (Phila Pa 1976), 2013;38(17):E1096-107.
47. Boselie TF et al. *WITHDRAWN: Arthroplasty versus fusion in single-level cervical degenerative disc disease.* Cochrane Database Syst Rev, 2015(5): p. CD009173.
48. Zechmeister I, Winkler R, Mad P. *Artificial total disc replacement versus fusion for the cervical spine: a systematic review.* Eur Spine J. 2011;20(2):177-84.

49. Verma K et al. *Rate of adjacent segment disease in cervical disc arthroplasty versus single-level fusion: meta-analysis of prospective studies.* Spine (Phila Pa 1976). 2013;38(26):2253-7.
50. Tetreault L et al. *Clinical and Surgical Predictors of Complications Following Surgery for the Treatment of Cervical Spondylotic Myelopathy: Results From the Multicenter, Prospective AOSpine International Study of 479 Patients.* Neurosurgery. 2015.
51. Lim S et al. *Predictors for Airway Complications Following Single- and Multi-level Anterior Cervical Discectomy and Fusion.* Spine (Phila Pa 1976). 2016.
52. Flynn TB. *Neurologic complications of anterior cervical interbody fusion.* Spine (Phila Pa 1976). 1982;7(6):536-9.
53. Fountas KN et al. *Anterior cervical discectomy and fusion associated complications.* Spine (Phila Pa 1976) 2007;32(21):2310-7.
54. Gruskay JA et al. *Factors Affecting Length of Stay and Complications After Elective Anterior Cervical Discectomy and Fusion: A Study of 2164 Patients From The American College of Surgeons National Surgical Quality Improvement Project Database (ACS NSQIP).* Clin Spine Surg. 2016;29(1):E34-42.
55. Nanda A. et al. *Surgical complications of anterior cervical diskectomy and fusion for cervical degenerative disk disease: a single surgeon's experience of 1,576 patients.* World Neurosurg. 2014;82(6):1380-7.
56. Riley LH Jr et al. *The results of anterior interbody fusion of the cervical spine. Review of ninety-three consecutive cases.* J Neurosurg. 1969;30(2):127-33.
57. Tew JM Jr, Mayfield FH. *Complications of surgery of the anterior cervical spine.* Clin Neurosurg. 1976;23:424-34.
58. Fehlings MG et al. Introduction: *Degenerative cervical myelopathy: diagnostic, assessment, and management strategies, surgical complications, and outcome prediction.* Neurosurg Focus. 2016;40(6):E1.
59. Veeravagu A et al. *Surgical outcomes of cervical spondylotic myelopathy: an analysis of a national, administrative, longitudinal database.* Neurosurg Focus. 2016;40(6):E11.
60. Tetreault L et al. *A systematic review of clinical and surgical predictors of complications following surgery for degenerative cervical myelopathy.* J Neurosurg Spine. 2016;24(1):77-99.
61. An HS, Jenis LG. *Complications of Spine Surgery: Treatment and Prevention.* 2006, Philadelphia: Lippincott Williams & Wilkins.
62. Ning X et al. *Anterior cervical locking plate-related complications; prevention and treatment recommendations.* Int Orthop, 2008;32(5):649-55.
63. Park JB, Cho YS, Riew KD. *Development of adjacent-level ossification in patients with an anterior cervical plate.* J Bone Joint Surg Am. 2005;87(3):558-63.
64. Brennan PA, Mahadevan V, Evans BT. *Clinical head and neck anatomy for surgeons.* 2015: CRC Press. xix, 338 pages.

BOOK REVIEW

Oxford Neurology Library: Alzheimer's Disease, second edition

The aim of this tiny reference book is to provide the clinician with a pocket size, comprehensive manual on diagnosis and management of Alzheimer's disease (AD). It is evidence-based and up-to-date; it encompasses the biology of AD, psycho-social aspects and brief discussion of differential diagnoses. The referencing is comprehensive. Key drug trials and other research studies are included and summarised. Each of the 14 chapters is written by an expert in that subject area.

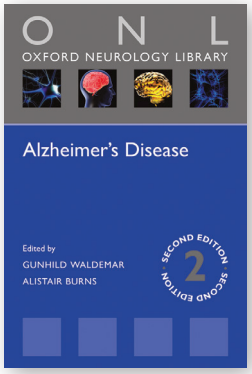
The book not only serves as a quick reference for practising clinicians but also offers guidance on multi-faceted aspects of management, relevant both to patients and their caregivers. It is designed to meet the needs of advanced medical students as well as doctors in neurology, psychiatry and general medicine.

The information is succinct and clearly written, being organised into chapters dealing with particular aspects of disease identification and/or management. The first chapter is an overview of dementia, describing the different types and their prevalence, and also the key presenting features. Subsequent chapters deal exclusively with Alzheimer's disease. The chapters are well structured and address current theories of pathophysiology, knowledge of the genetics in familial forms of the disease and risk factors for sporadic disease, epidemiology, presenting features diagnosis and how to communicate a diagnosis to a patient. A holistic view of management is also provided. Pharmacological treatments, end of life care, social care and safety, legal issues and driving are all discussed. The concluding sections of each chapter identify any areas of research gaps in the field and avenues of possibility for further exploration.

The last chapter outlines various cases to illustrate and emphasise key concepts.

In terms of format, the information within each chapter is arranged under a main heading and then various subheadings. This assists the reader when looking for a specific topic. At the beginning of each chapter there is a list of key points or take home messages that should be gleaned from the chapter. There are some illustrations and images included but these are mainly black and white; they are of varying use and appeal. Colour print could have enhanced the illustrations and provided more clarity but additional costs, no doubt. The very small print lends itself to using the book as a mini-reference rather than a mini-introduction to be read from cover to cover. In any case, there is too much medical terminology for it to be recommended to a lay person or, say, a non-clinical scientist.

The purpose of the book is to provide a quick and easily accessible reference text and update for clinicians working in this field or for those new to the profession. I feel that the authors have succeeded in doing this. The book is small and easily transportable and is not too expensive.



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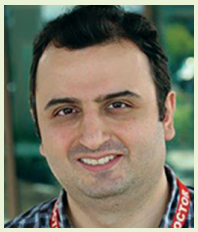

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Professor Broadley has received grants, and personal fees from Biogen Novartis,Merck-Serono, Sanofi-Genzyme, Alexion, Bayer-Schering, and TEVA. He was the lead author of a series of articles providing guidance on the treatment of MS in Australia and New Zealand and is the chair of the Research Management Committee of Multiple Sclerosis Research Australia and the Chair of the MS Neurology Group of the Australian and New Zealand Association of Neurologists.

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Neuromyelitis Optica Spectrum Disorder

Key Points

- NMOSD is a distinct pathological entity due to antibodies to aquaporin 4
- NMOSD presentations are due to a predilection of this pathology for the optic nerve, spinal cord and periependymal regions of the brain
- NMOSD has typical MR imaging features and antibodies to aquaporin 4 are usually positive
- Early agressive treatment of relapses in NMOSD minimises accrual of disability
- Preventive treatment is recommended for confirmed cases of NMOSD

Abstract
Over the past 13 years neuromyelitis optica spectrum disorder (NMOSD) has emerged as a discrete form of demyelinating disease of the central nervous system in which antibodies against a water channel found in high concentration on astrocytes are frequently found. Following the discovery of this pathogenic antibody the phenotype of this condition, previously known as Devic's disease, has broadened from one of monophasic or recurrent, optic neuritis and transverse myelitis, to include area postrema lesions, hypothalamic lesions and a fulminant encephalopathic presentation. Clues to the diagnosis include clinical presentations related to the above locations of pathology and imaging changes including longitudinally extensive spinal cord lesions, extensive optic nerve lesions, particularly lesions posterior to or involving the chiasm, and reactive cerebrospinal fluid. Early identification of this disorder is important as the prognosis without treatment is poor and generally worse than is seen in multiple sclerosis (MS). In addition, the approach to treatment (immunosuppression and anti-B-cell therapy) is different to MS and there is a concern that some disease modifying therapies that are helpful in MS may be harmful in NMOSD.

Introduction

Neuromyelitis optica spectrum disorder (NMOSD) is an antibody-mediated, inflammatory disease of the central nervous system primarily affecting the optic nerves, spinal cord and periependymal regions of the cerebral hemispheres and brainstem.[1] Following the initial descriptions of what became known as Devic's disease, monophasic, sequential and relapsing forms of a distinct pathological entity with a predilection for the optic nerves and spinal cord had been recognised for over a century.[2] The discovery of antibodies against the aquaporin 4 (AQP4) water channel in 2004 has enabled a broadening of the phenotype of this astrocytopathy to include a core group of six clinical syndromes.[3]

Pathogenesis

Antibodies to AQP4 play a key role in the pathogenesis of NMOSD.[4] AQP4 is a water channel that is predominantly expressed on the cell membrane of astrocytic end-feet, forming part of the blood–brain barrier. Predilection for particular regions of the CNS in NMOSD is related to higher expression of AQP4 in the optic nerves and spinal cord and a lack of tight junctions between endothelial cells forming a permeable blood-brain barrier in these areas.[1] Binding of antibody downregulates AQP4 and causes astrocytic injury through activation of the classical complement pathway. Antibody-complement complex formation results in chemotaxis of T and B lymphocytes, macrophages, neutrophils and eosinophils, principally through activation of NFκB.[4] Demyelination and oligodendrocyte injury occur as a secondary effect of this immune response.[1] This pathological picture is distinct from and more destructive than that seen in MS. The main pathological features of NMOSD are illustrated in Figure 1.

Epidemiology

The incidence of NMOSD ranges from 0.053 to 0.4 per 100,000 individuals with prevalence rates from 0.52 to 4.4 per 100,000.[5] NMOSD is more prevalent among non-Caucasians and is relatively rare in childhood.[5] Onset is more evenly spread across the adult age range than is seen in MS and the mean age at onset is higher (40-45 vs. 30-35 years).[5]

Clinical Features

The common presenting features of NMOSD can be attributed to lesions of the optic nerve, spinal cord, area postrema, periependymal regions of the third ventricle and hypothalamus, brainstem and cerebral hemispheres.[3] The typical clinical presentations of NMOSD are given in Table 1. The key to recognising NMOSD as the diagnosis in patients presenting with demyelinating disease of the central nervous system is the early identification of the listed clinical and radiological features for each type of presentation and having a low threshold for requesting AQP4 antibody testing.

Clinical Course and Prognosis

The majority of NMOSD patients have a relapsing disease course and the presence of AQP4 antibodies is predictive of a relapsing course in limited forms of the disease (e.g. monophasic transverse myelitis). Unlike MS, a secondary progressive phase is uncommon in NMOSD.[6] However, significant permanent disability resulting from acute attacks due to frequently necrotic pathology is common in NMOSD.[3] As a consequence the prognosis without treatment in NMO is generally worse than for MS.

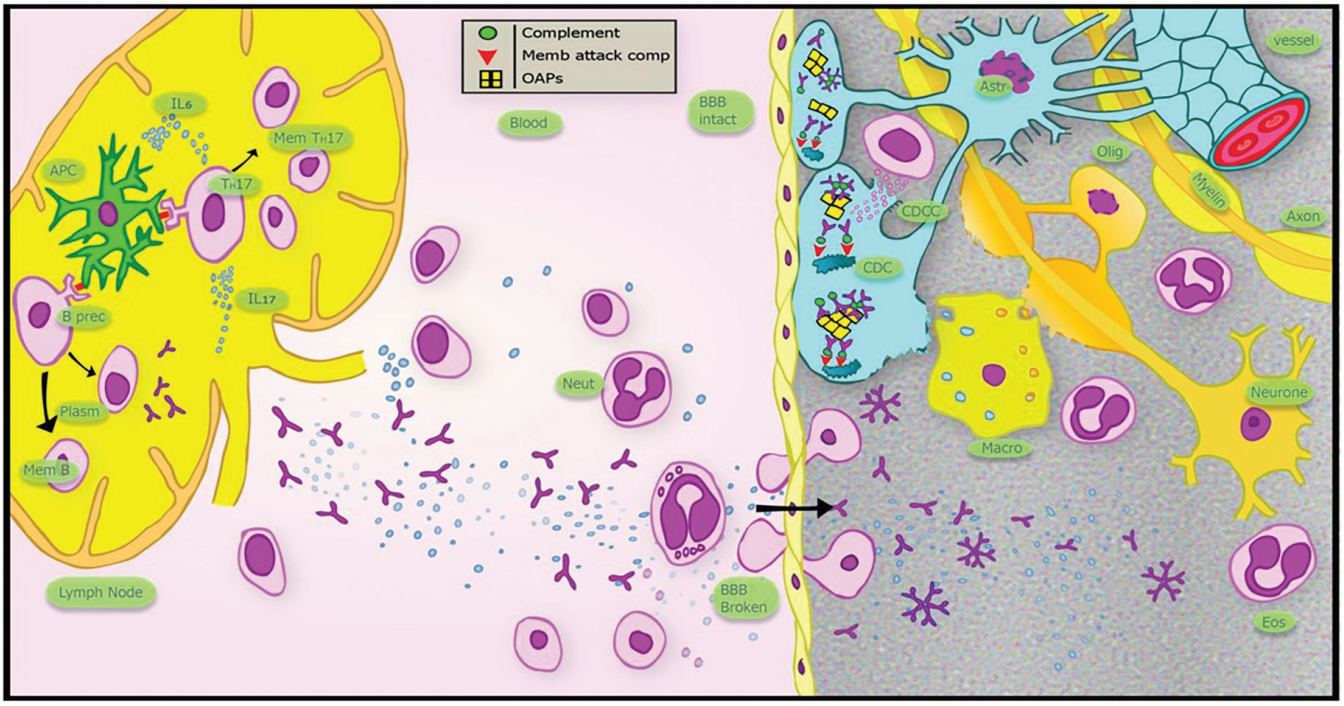

Figure 1. Schematic representation of NMOSD pathology. APC = antigen presenting cell; B prec = precursor B cell; Plasm = Plasma cell; Mem B = memory B cell; Mem Th17 = memory Th17 cell; Neut = neutrophil; BBB = blood brain barrier; CDC = complement dependant cytotoxicity; CDCC = complement dependant cell mediated cytotoxicity; Astr = astrocyte; Olig = oligodendrocyte; Macro = macrophage; Eos = eosinophil. Reproduced with permission.

Table 1: Clinical Features of NMO and Wingerchuk 2015 Diagnostic Criteria

Core Clinical Presentation	Typical Presentation	Seropositive criteria	Seronegative criteria	Additional Imaging Requirements (seronegative cases only)
Optic Neuritis	Bilateral Sequential Severe Poor Recovery Painless	At least one core presentation + Positive AQP4 antibodies	At least one of these + At least one other core presentation + Additional imaging Requirements as listed	Optic Neuritis with (1) normal MR imaging of brain or non-specific white matter lesions, or (b) T2 or T1 GAD-enhancement of optic chiasm or at least ½ optic nerve length on MR imaging of orbits
Acute Myelitis	Bilateral Motor Sensory Sphincter involvement			Longitudinally extensive spinal cord lesion (or atrophy) ≥ 3 vertebral segments on MR imaging of spine
Area Postrema Syndrome	Persistent vomiting Nausea Hiccoughs			Area postrema lesion on MR imaging of brain
Acute Brainstem Syndrome	Cranial Palsies Ataxia Limb weakness			Periependymal brainstem lesion on MR imaging of brain
Diencephalic Syndrome	Narcolepsy Hypothermia Daytime somnolence Obesity			
Cerebral Syndrome	Encephalopathy Seizures			

Associated Autoimmune Disease

Around 20 – 30% of NMOSD patients have a co-existing autoimmune disease and autoantibodies other than anti-AQP4 can be detected in up to 40%.[7] Case reports of NMOSD being associated with cancer suggest that the disease may occasionally occur as a paraneoplastic phenomenon.[7]

Diagnosis and Investigations

In 2015 The International Panel for NMO Diagnosis unified the concept of NMO and NMOSD and developed the revised diagnostic criteria based on AQP4-IgG status in which more strict clinical criteria, with additional neuroimaging findings are required for diagnosis of NMOSD when AQP4 antibodies are absent or where serologic testing is unavailable.[3] The key elements of these criteria are given in Table 1.

Imaging

The most distinct manifestation of NMOSD is a longitudinally extensive spinal cord lesion, defined as a lesion that spans over three or more contiguous vertebral segments and predominantly involves central grey matter.[8] Non-specific, white matter, dots and patches of T2/FLAIR hyperintensity are the most common findings on MR images of the brain in NMOSD.[8] Lesions in the dorsal brainstem adjacent to the fourth ventricle including the area postrema and the nucleus tractus solitarius are more specific for NMOSD. Other typical brain lesions include bridging lesions of the splenium, and periependymal lesions of the ventricles and aqueduct. Lesions of the corpus collosum tend to be more heterogeneous than those seen in MS. Lesions of the corticospinal tracts may also be seen.[8] Increased signal within the optic nerve may be detected with fat suppressed T2-weighted orbital MRI sequences, typically with gadolinium enhancement seen on T1-weighted sequences. Bilateral optic nerve involvement, posterior nerve predominance (especially with extension into the optic chiasm), or extensive lesions of the optic nerve (more than half of its length) are all suggestive of NMOSD.[3] Typical MR imaging appearances of NMOSD are shown in Figure 2.

Serological Testing

Anti-AQP4 antibodies

Antibodies against AQP4 are detected in a high proportion of patients with NMOSD (70 – 80%).[9] A number of different assays are available, including immunofluorescent histological techniques, enzyme-linked immunosorbent assay (ELISA), dried cell-based assays and live cell-based assays with and without fluorescence assisted cell sorting. Evidence suggests that the live-cell based assays are the most sensitive.[9] All appear to be highly specific (97% or higher) with the exception of ELISA methods. ELISA can be useful in providing a ready measure of the antibody titre.[9] Many laboratories use a combination of techniques to improve sensitivity and specificity.

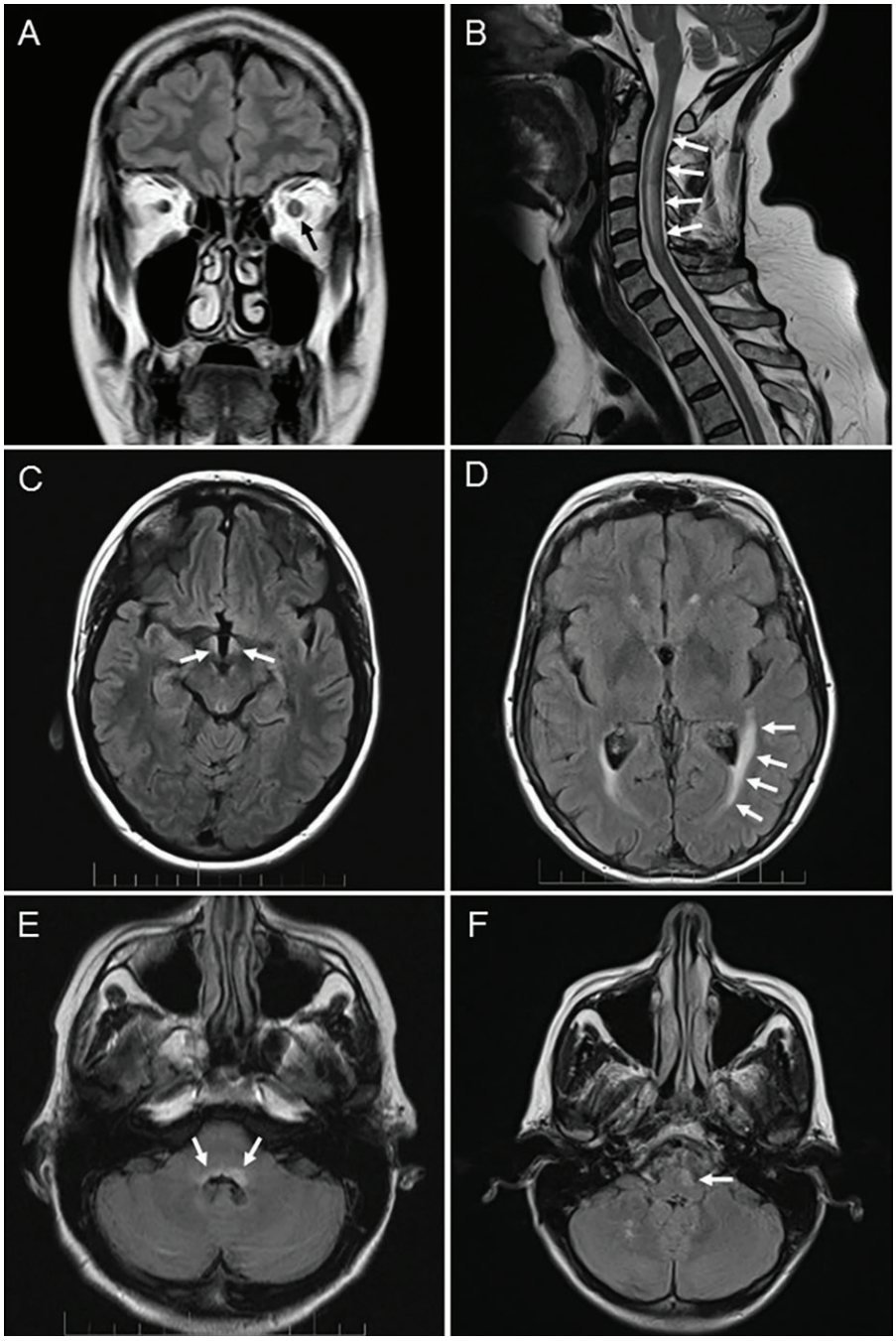

Figure 1. Schematic representation of NMOSD pathology
APC = antigen presenting cell; B prec = precursor B cell; Plasm = Plasma cell; Mem B = memory B cell; Mem Th17 = memory Th17 cell; Neut = neutrophil; BBB = blood brain barrier; CDC = complement dependant cytotoxicity; CDCC = complement dependant cell mediated cytotoxicity; Astr = astrocyte; Olig = oligodendrocyte; Macro = macrophage; Eos = eosinophil.
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Anti-MOG antibodies

The finding of antibodies targeted against myelin oligodendrocyte glycoprotein (MOG) in a small proportion of AQP4 seronegative NMOSD has raised the question of whether or not these patients form a subgroup of NMOSD. However, an emerging phenotype of ADEM in childhood and recurrent optic neuritis or classical Devic's presentation (simultaneous optic neuritis and acute myelitis) in adolescence and adults is defining this condition as a separate demyelinating disease which has been coined 'anti-MOG related demyelinating disease'.[10] A typical MR imaging feature of this condition is a longitudinally extensive spinal cord lesion extending all the way down to the conus. The optic neuritis in this condition is typically highly steroid sensitive.

Other Investigations

Elevation of cerebrospinal fluid (CSF) protein and CSF pleocytosis are more commonly seen during acute attacks of NMOSD and are of some assistance in distinguishing NMOSD from MS.[11] In MS, a CSF white cell count greater than 10 per ml is rare. Oligoclonal bands in the CSF are seen less often than in MS, but can be present in up to 20% of patients with NMOSD.[11]

Somatosensory evoked potentials, brainstem acoustic evoked potentials and visual evoked potentials are frequently abnormal when symptomatic lesions are tested in NMOSD, but unlike MS asymptomatic abnormalities are rare[12] and there is no evidence for peripheral motor and sensory nerve conduction abnormalities in NMOSD.[13]

Optical coherence tomography in NMOSD shows significantly greater retinal nerve fibre layer thinning than is typically seen in MS, reflecting a more severe axonal injury.[14] It has been proposed that this may be a useful indicator for potential NMOSD cases, but these changes may take several weeks or even months to become established following an acute attack of optic neuritis.

Treatment

Acute exacerbations should be treated promptly with high-dose intravenous methylprednisolone for 3-5 days. Most authors recommend a subsequent taper of oral prednisolone over 2-3 months to prevent relapse, particularly when the level of deficit at presentation is high. The period of oral steroids can be adjusted in the light of other adjunctive therapies. Where immediate improvement is not seen, a low threshold for the early implementation of plasma exchange is recommended. Indeed, many would advocate immediate plasma exchange when initial neurological impairment is severe (e.g. paraplegia), in order to optimise recovery.[11]

For the prevention of relapses azathioprine, mycophenolate mofetil and rituximab are recommended. There are no randomised, placebo controlled or head-to-head comparison trials of these agents in NMOSD, but rituximab may have greater efficacy.[11] Mycophenolate mofetil has fewer and milder adverse events compared with azathioprine with similar efficacy.[15]

Where doubt exists regarding the diagnosis of NMOSD or MS (e.g. clinical or radiological features suggestive of NMOSD in a seronegative patient with MR imaging of brain that is not typical of MS) then treatment with β-interferon, fingolimod and natalizumab should be avoided as there is some evidence to suggest that these therapies may have a negative outcome in NMOSD.[16] Glatiramer acetate does not have this drawback and there is some evidence to suggest it may be helpful in NMOSD and anti-B-cell therapies in the form of rituxumab or ocrelizumab have evidence of efficacy in both MS and NMOSD.

Conclusions

NMOSD represents a distinct clinical and pathological entity which has some clinical overlap with MS, optic neuritis and transverse myelitis, but can now be regarded as a unique astrocytopathy. The distribution of AQP4 and the activation of complement explains both the clinical phenotypic expression of the disease and its severity. A high degree of clinical suspicion with any clinical or MR imaging features of NMOSD is crucial for early diagnosis. Aggressive treatment of acute relapses and early adoption of long term preventive therapies are key to minimising the long term adverse outcomes that have been a hall mark of this condition in the past.

REFERENCES

1. Lucchinetti CF, Guo Y, Popescu BF, et al. *The pathology of an autoimmune astrocytopathy: lessons learned from neuromyelitis optica.* Brain Pathol 2014;24(1):83-97.
2. Wingerchuk DM, Hogancamp WF, O'Brien PC, et al. *The clinical course of neuromyelitis optica (Devic's syndrome).* Neurology 1999;53(5):1107-14.
3. Wingerchuk DM, Banwell B, Bennett JL, et al. *International consensus diagnostic criteria for neuromyelitis optica spectrum disorders.* Neurology 2015;85(2):177-89.
4. Bukhari W, Barnett MH, Prain K, et al. *Molecular pathogenesis of neuromyelitis optica.* Int J Mol Sci 2012;13(10):12970-93.
5. Pereira WL, Reiche EM, Kallaur AP, et al. *Epidemiological, clinical, and immunological characteristics of neuromyelitis optica: A review.* J Neurol Sci 2015;355(1-2):7-17.
6. Wingerchuk DM, Pittock SJ, Lucchinetti CF, et al. *A secondary progressive clinical course is uncommon in neuromyelitis optica.* Neurology 2007;68(8):603-5.
7. Iyer A, Elsone L, Appleton R, et al. *A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitis optica.* Autoimmunity 2014;47(3):154-61.
8. Kim HJ, Paul F, Lana-Peixoto MA, et al. *MRI characteristics of neuromyelitis optica spectrum disorder: an international update.* Neurology 2015;84(11):1165-73.
9. Ruiz-Gaviria R, Baracaldo I, Castaneda C, et al. *Specificity and sensitivity of aquaporin 4 antibody detection tests in patients with neuromyelitis optica: A meta-analysis.* Multiple sclerosis and related disorders 2015;4(4):345-9.
10. Ramanathan S, Dale RC, Brilot F. *Anti-MOG antibody: The history, clinical phenotype, and pathogenicity of a serum biomarker for demyelination.* Autoimmun Rev 2016;15(4):307-24.
11. Flanagan EP, Weinshenker BG. *Neuromyelitis optica spectrum disorders.* Curr Neurol Neurosci Rep 2014;14(9):483.
12. Ohnari K, Okada K, Takahashi T, et al. *Evoked potentials are useful for diagnosis of neuromyelitis optica spectrum disorder.* J Neurol Sci 2016;364:97-101.
13. Sellner J, Boggild M, Clanet M, et al. *EFNS guidelines on diagnosis and management of neuromyelitis optica.* Eur J Neurol 2010;17(8):1019-32.
14. Bennett JL, de Seze J, Lana-Peixoto M, et al. *Neuromyelitis optica and multiple sclerosis: Seeing differences through optical coherence tomography.* Mult Scler 2015;21(6):678-88.
15. Chen H, Qiu W, Zhang Q, et al. *Comparisons of the efficacy and tolerability of mycophenolate mofetil and azathioprine as treatments for neuromyelitis optica and neuromyelitis optica spectrum disorder.* Eur J Neurol 2017;24(1):219-26.
16. Kira JI. *Unexpected exacerbations following initiation of disease-modifying drugs in neuromyelitis optica spectrum disorder: Which factor is responsible, anti-aquaporin 4 antibodies, B cells, Th1 cells, Th2 cells, Th17 cells, or others?* Mult Scler 2017:1352458517703803.

Edward Nettleship and Optic neuritis

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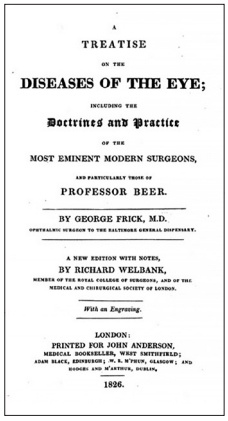
Abstract
Arabic texts of the ninth century described loss of sight as one form of ocular paralysis. Some early descriptions of amaurosis in retrospect probably describe optic neuropathy but its nature and defining physical signs arose from Helmholtz's ophthalmoscope in 1845. In 1864 von Gräfe and later Thomas Buzzard and Clifford Allbutt gave detailed accounts, but the most important description was the 1884 work of the ophthalmologist Edward Nettleship, which is here recounted.

Optic neuritis, often named retrobulbar neuritis or optic papillitis, is one of the commonest symptoms of multiple sclerosis (MS). At some stage it affects over 50% of MS patients. An early description in 1864 was by Albrecht von Gräfe [Graefe] (1828-1870).[1] Modern techniques made diagnosis easier and more precise, but the early descriptions and much-argued concepts are seldom discussed. A thinning of the serial ganglion cell layer and inner plexiform layer is the pathogenesis of acute optic neuritis.

Ancient references to optic nerve dysfunction as a mechanism for loss of vision are found in Arabic texts of the ninth century.[2] Possibly the first textbook of ophthalmology was written by Hunayn ibn Ishaq, (808-873) a Nestorian Christian and chief physician to the Caliph al-Mutawakkil. Like Galen, he believed that the optic nerve was hollow to transmit psychic *pneuma** that flowed from the brain; the lens was the organ of vision. This he deduced by shutting one eye, whereupon the pupil of the other became enlarged to allow the escape of diverted pneuma. When the closed eye was opened, the enlarged pupil contracted to normal size.[3] He described three different forms of ocular paralysis: those involving sight alone, those involving eye movements alone, and those involving both; but he failed to separate optic neuritis from other eye diseases:

> The vision has ceased or diminished without our finding any change in the pupil and there is heaviness in the head and particularly its deep part and the parts surrounding the orbit. We know that the affection is caused by abundant moisture, which has run to the optic nerve…

Even before von Gräfe, in December 1822, Sir Augustus D'Este, grandson of King George III., when he was 28 years old, suffered what in retrospect was an attack of retrobulbar neuritis, though its nature was not realised at the time. In successive years, he noted progressive weakness, numbness, difficulty in walking, painful spasms and depression — all typical of MS.[4,5] Although he was aged 54 when he died, no formal diagnosis was made, but 'the meticulous notes in his diary justify a posthumous diagnosis'.[5]


A
TREATISE
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1826.

Fig 1. Frick's Treatise on the Diseases of the Eye.

In 1823, George Frick (1793-1870)[4] in the first American textbook (Figure 1) of ophthalmology (1823) had described varieties of amaurosis that included but did not demarcate optic neuritis:

> "The terms *amaurosis, gutta serena, suffusion nigra, &c* are applied to a species of blindness which is produced by some immediate affection of the optic nerve or its expansion into the retina ... Amaurosis may take place suddenly or slowly and be transient, permanent or intermittent." (Pp.138-141. 1826 edition)

But before the ophthalmoscope, Frick was unable clearly to distinguish optic neuritis from uveitis, glaucoma, orbital tumours, and other eye and systemic disorders. Shrewdly, he had noted severe pain in the orbit before visual loss and abnormal pupillary responses to light. He related:

> Amaurosis from whatever cause ... is generally characterized by a very dilated pupil which is not affected by any degree of light which is made to fall upon the retina ... [the patient] is obliged to turn his head to render them [objects] distinct. (p. 142)

The invention of the ophthalmoscope by Hermann von Helmholtz (1821–1894): in 1845[5,6] allowed optic neuritis to be separated from many other ocular disorders. So valuable was the ophthalmoscope that by 1871, Thomas Clifford Allbutt[8] (1836–1925) protested:

> The number of physicians who are working with the ophthalmoscope in England may, I believe, be counted upon the fingers of one hand'.

And in this seminal text, he recognised the salient features of optic neuritis and 'atrophic amaurosis' and the frequent confusion with ischaemic optic neuropathy.[7]

In 1860 von Graefe ((1828–1870),[8] and more meticulously, Edward Nettleship (1845-1913) in 1884 described its principal features.[9] Nettleship acknowledged that both Leber and Jonathan Hutchinson had previously described cases of optic neuritis. However, Leber included instances of tobacco amblyopia and Hutchinson included several other pathologies. Nettleship's comprehensive account in 1884 emphasised pain on eye movement, abnormal disk appearances and he stressed the impaired colour vision. Eleven of his 16 patients had a central scotoma. He accurately characterised its features:

> Failure of sight limited to one eye, often accompanied by neuralgic pain about the temple and orbit and by pain in moving the eye; many recover but permanent damage and even total blindness may ensue; there is at first little, sometimes no, ophthalmoscopic change, but the disc often becomes more or less atrophic in a few weeks… The defect in vision is often described at first as a "gauze" or a "yellow mist" or a "dark patch" or a "spot" which covers the object looked at and gives an unnatural colour, the hand looking, for example, as if covered by a brown glove.'

Although he identified all the salient features of optic neuritis, he did not mention a relationship to other relapsing and remitting neurologic symptoms, characteristic of MS. In the 19th century, optic neuritis was often used as a descriptive term for papilloedema. Its most common cause was widely said to be a brain tumour. It was also recognised as a discrete disease of the optic nerves,[9] though its aetiology was often uncertain.

After Nettleship's seminal description, Thomas Buzzard (1831-1919)† (Figure 2.) in 1893 reported five patients with a history of disseminated sclerosis, who had episodes of visual failure with recovery consistent with optic neuritis.[10] He was one of the first to recognise optic atrophy as a feature of disseminated (multiple) sclerosis.


SECTION OF OPHTHALMOLOGY.
ATROPHY OF THE OPTIC NERVE AS A SYMPTOM OF CHRONIC DISEASE OF THE CENTRAL NERVOUS SYSTEM.

Fig 2. Buzzard T. Atrophy of the optic nerve

He credited Charcot with the first description of *Sclérose en plaques* and for noting amblyopia as a frequent symptom.[11] Parinaud[12] had noted the impairment of colour vision in optic neuritis, and later James Adie re-emphasised the importance of a central or paracentral scotoma,[13] which he regarded as essential for diagnosis.

Wilhelm Uhthoff (1853–1927),[14] a *Privatdocent für Augenheilkunde* in Berlin, in 1890 described characteristic, transient blurring of central vision on exercise, rise in temperature, and fatigue in disseminated sclerosis, known as Uhthoff's sign.

Neuromyelitis optica (Devic's disease)

In 1870, (Sir) Thomas Clifford Allbutt, then Physician to the General Infirmary at Leeds, first reported the association between myelitis and an optic nerve disorder.[15] He briefly described a case of myelitis followed by optic neuritis approximately three months later. Earlier, EO Hocken had reported a patient with spinal cord inflammation and amaurosis in 1841.[16] CM. Durrant described a probable case in 1850.[17] Wilhelm Erb in 1879 described a man who developed recurrent optic neuritis succeeded by subacute myelitis.[18] Dreschfeld in 1882 described the first pathologically examined case[19] and showed inflammation in both the spinal cord and optic nerves; the brain was normal. In 1894, Eugène Devic (158-1930)[20] presented his case at the First Congress of Internal Medicine in Lyon, and with Gault summarised 16 patients with loss of vision, who within weeks developed spastic paresis. Devic's telling question, 'Why such a peculiar localisation?' remains unanswered. Neuromyelitis optica (NMO) has well known similarities to multiple sclerosis, but despite the finding of NMO-IgG (Aquaporin 4) in about two-thirds of cases of NMO, whether it is an Aquaporin 4 + NMO autoimmune astrocytopathy, a disease sui generis, or an MS variant remains arguable.[21]

In typical optic neuritis, visual function improves spontaneously over four to six weeks, and within 12 months 93% have acuity of at least 20/40. High-dose corticosteroids may hasten recovery, but have little effect on long-term visual outcome. The cumulative probability of developing MS by 15 years is 50%. White matter plaques on the first magnetic resonance image increase that risk to 72%.

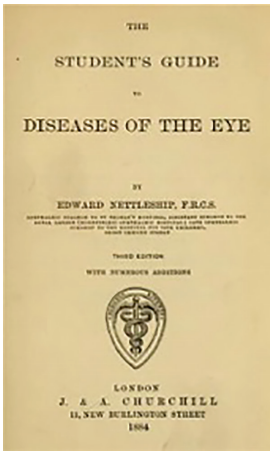
Edward Nettleship (1845-1913)

Of the many who contributed to the descriptions of optic neuritis it is Nettleship whose comprehensive writings first clearly delineated the disorder. Born on 3 March 1845 in Kettering, Northamptonshire, he attended Kettering grammar school. Intending at first to become a farmer, he entered King's College, London, and the Royal Veterinary College, and was admitted a Licentiate of the Society of Apothecaries and received the diploma of the Royal College of Veterinary Surgeons in 1867. He was appointed Professor of Veterinary Surgery at the Royal Agricultural College but a year later returned to the London Hospital, as dresser and assistant to (Sir) Jonathan Hutchinson.[22] Nettleship became his firm friend, and most distinguished pupil. He qualified in surgery (F.R.C.S.), from the London Hospital and the Blackfriars Hospital for Skin Diseases. To specialise in ophthalmology, in 1868, he studied at Moorfields Eye Hospital under Hutchinson and Waren‡ Tay. He was appointed Curator of the Museum and Librarian.

On 22 January 1869 he married Elizabeth Endacott Whiteway from Devon; they had no children. At Moorfields he began his researches into eye diseases,[23] but left for the post of medical superintendent at the Ophthalmic School at Bow (1873–4), working with impoverished children suffering from eye infections, He was then appointed ophthalmologist at the South London Ophthalmic Hospital, St Thomas's Hospital (1878–95), and surgeon at Moorfields (1882–98). In 1888 he became Dean of the Medical School. He served and became President of the Ophthalmological Society, and advised the Board of Trade on Sight Tests for the Mercantile Marine.

Nettleship acquired a considerable reputation as an eye surgeon and teacher. Sir John Parsons described him as the most scientific teacher of his time. He removed a cataract from William Ewart Gladstone, and attended Queen Victoria for the same condition, but advised against surgery.

Whilst working at St Thomas's and Moorfields Eye hospital, he wrote the definitive text: *The Student's Guide to Diseases of the Eye* (Figure 3.) that ran to five editions. His *On Some Hereditary Diseases of the Eyes*, 1909 was the standard monograph. His studies on hereditary eye diseases: albinism, retinitis pigmentosa, were executed mainly in 'retirement' in 1902 to Hindhead; there he concentrated on a pioneering series of papers on hereditary eye disease which was recognised in 1912 by Fellowship of the Royal Society. Nettleship, a shy, reserved man, attracted many disciples to his clinic, who were keen to learn his methods, and to submit to his somewhat severe discipline. But his patients and friends readily appreciated his underlying kindness and generosity. Prostatic surgery in 1911 led to distressing complications, accompanied by colonic carcinoma. Despite radiotherapy, he died at his home, in Hindhead, Surrey, on 30 October 1913. The Ophthalmological Society awards the Edward Nettleship Prize triennially; the first was to Nettleship himself in 1909 in recognition of his researches.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EDWARD NETTLESHIP, F.R.C.S.
LONDON
J. & A. CHURCHILL
11, NEW BURLINGTON STREET
1884

Fig 3. Nettleship's The Student's guide to Diseases of the Eye. (1884 ed'n)

* Pneuma: metaphorical breath of life

† One of his sons was Sir Farquhar Buzzard, Bart, F.R.C.P, who followed in his footsteps as physician to the National Hospital, Queen Square

‡ Usually misspelt Warren

REFERENCES

1. von Gräfe ' Klin, Monatsbl f Augeuh, i, 49 cited In: *Clinical lecture on a case of retro-bulbar abscess.* Medicine, Surgery, And Their Allied Sciences. The New Sydenham Society. London. MDCCCLXIV. p. 267
2. Volpe NJ. *Optic Neuritis: Historical Aspects.* Journal of Neuro-Ophthalmology 2001;21(4):302-9.
3. Hunain ibn Is-hâq. *The Book of the Ten Treatises on the Eye,* Publisher: English translation and glossary by Max Meyerhof Government Press: Cairo, 1928.
4. Frick G. *A treatise on the diseases of the eye.* Baltimore: Fielding Lucas; 1823.
5. Helmholtz H. *Beschreibung eines Augen-Spiegels.* Berlin, Germany: A Förstner'sche Verlagsbuchhandlung; 1851.
6. Pearce J.M.S. The Ophthalmoscope: Helmholtz's Augenspiegel. Eur Neurol 2009;61:244–9.
7. Allbutt TC, Allbutt T. *On the ophthalmoscopic signs of spinal disease.* Lancet 1870;I:76-8.
8. von Graefe A. *Ueber complication von sehnervenentzundung mit gehirnkrankheiten.* Archiv Ophthalmologic 1860;1:58-71.
9. Nettleship E. *On cases of retro-ocular neuritis.* Trans Ophthal Soc UK 1884;4:186-226.
10. Buzzard T. *Atrophy of the optic nerve as a symptom of chronic disease of the central nervous system.* Br Med J 1893;2:779-784.
11. Charcot JM. *Histologie de la sclérose en plaques.* Gaz Hop (Paris) 1868;41:554, 557–8, 566.
12. Parinaud H. *Troubles oculaires de la sclerose en plaques.* J Sante 1884;3:3-5.
13. Adie W J. *The aetiology and symptomatology of disseminated sclerosis.* British Medical Journal 1932;2:997-1000.
14. Uhthoff W. *Untersuchungen uber die bei der multiplen herdskle- rose vorkommenden augenstorungen.* Arch Pyschiat NervKranken 1890;21:55-116, 303-410.
15. Allbutt T. *On the ophthalmoscopic signs of spinal disease.* Lancet 1870;I:76-8.
16. Hocken E (1841) *Illustrations of the pathology and treatment of the amauroses. Amaurosis from affections of the spinal cord or its membranes.* London Medical Gazette 707. XXVIII. New Series. Vol. II. 1840–41:499–504. Cited by Jarius, S. & Wildemann, B. J Neurol (2014) 261: 400. doi:10.1007/s00415-013-7210-x
17. Jarius S, Wildemann B. *An early case of neuromyelitis optica (1850: Provincial Medical and Surgical Journal).* Brit Med J 2012;345:e6430.
18. Erb W. *Uber das Zusammenkommen von Neuritis optica und Myelitis subacute.* Arch Psychiatr Nervenkr 1879;1:146-57.
19. Dreschfeld J. *Pathological contributions on the course of the optic nerve fibres in the brain.* Brain 1882;4:543-51. 23
20. Devic E. *Myelite subaigue compliquee de neurite optique.* Bull Med. 1894;8:1033–4.
21. Weinshenker BG, Wingerchuk DM. *The two faces of neuromyelitis optica.* Neurology February 11, 2014 vol. 82 no. 6 466-7.
22. Plarr's Lives of the Fellows Online. Nettleship, Edward (1845 - 1913)
23. Branford WA. *'Nettleship, Edward (1845–1913)'*, Oxford Dictionary of National Biography, Oxford University Press, 2004 [http://www.oxforddnb.com/view/article/35201, accessed 29 April 2017]
24. Bukhari W, Prain KM, Waters P, et al *Incidence and prevalence of NMOSD in Australia and New Zealand.* J Neurol Neurosurg Psychiatry Published Online First: 26 May 2017. doi: 10.1136/jnnp-2016-314839.

THE MISSING PIECES

IDENTIFYING GAPS IN CARE & CONVERSATIONS IN MULTIPLE SCLEROSIS

SANOFI GENZYME

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FOREWORD

Multiple sclerosis (MS) is an unpredictable, progressive, neurological condition in which the body's own immune system attacks the nerves in the central nervous system (the brain and spinal cord). Its severity and symptoms **differ from one person to the next, but anyone with MS will need care, intervention and support** throughout their lives to varying degrees.

With a progressive condition like MS, receiving the right treatment and care as early on as possible is critical to ensuring the best outcome, but in the UK people with MS still face challenges in accessing both specialist care and treatment.[1,2,3,4]

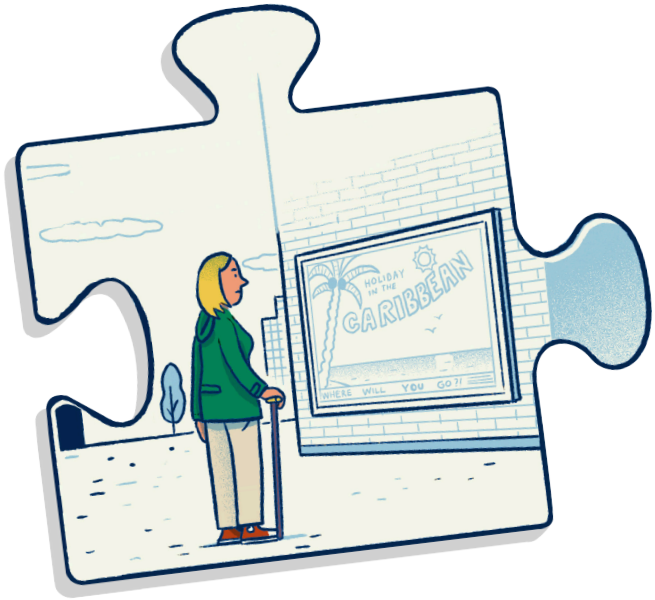
The most prevalent form of MS is relapsing remitting ms (RRMS). People with RRMS experience clinical attacks (relapses) when symptoms flare up or worsen, when the relapse is resolved then the person enters a period of remission. Treatment is primarily focussed on reducing the frequency of relapses, however, given that MS attacks the central nervous system which controls the body's movement, muscle action and balance, **research suggests that it's the impact of the disease on their ability to live their lives that's the key concern for people with MS.** People with MS struggle with both the uncertainty of unpredictable relapses and trying to remain free from disability for as long as possible.

Available treatments, known as Disease Modifying Treatments (or DMTs) can reduce the frequency of relapses and newer treatments have also been proven to delay the onset of disability. **However, in the UK only 21% of people with MS receive a DMT,** one of the lowest treatment rates in Europe.[5]

This report, which explores the attitudes of both people with MS and their healthcare professionals towards treatment of the disease in the UK, underlines the need to challenge our thinking around treatment goals and end-points. If maintaining their ability to live their daily lives as normally as possible is what's most important to people with MS, **then we need not only to reduce the frequency of relapses, but have the prevention of disability as a key treatment goal.**

This means in turn that we need to ensure everyone with MS has access, as early as possible, to treatments that can change the course of their disease.

In addition to this fundamental requirement, people with MS should also have access to a full range of support from a multidisciplinary team of professionals, plus a regularly reviewed personalised care plan (in line with the National Institute for Health and Care Excellence (NICE) Quality Standards for MS).[6] Unfortunately in the UK, as this report demonstrates, this is not always the case. **There are "missing pieces" which means that many people with MS are missing out on the treatments and care plan that could both help deliver on their quality of life goals and best meet their clinical needs.**



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INTRODUCTION

Sanofi, a global healthcare leader, and its specialty care business unit, Sanofi Genzyme, strives to be a long-term partner to the MS community by delivering scientific advances that will help meet the needs of people living with MS.

Sanofi Genzyme has launched an ongoing global campaign 'vs. MS', which aims to shed light on and address the true physical and emotional impact of MS. The 'vs.MS' campaign challenges us all to think beyond the commonly understood symptoms of MS and focusses on what real MS-related disability is - what it looks like, how it feels to have MS and how it impacts everyday living.

Retention of ability/delaying disability has emerged as the major issue coming out of the 'vs.MS' campaign. It is one of the key areas raised by people with MS, their partners and carers. 83% of respondents living with RRMS reported that what matters most to them is taking action to prevent progression and potential disability*.[7]

Missing Pieces is a UK specific campaign that builds on these findings. It sets out to further explore attitudes, understanding and behaviours around the treatment of MS in the UK. The objective is to identify the gaps in knowledge, awareness, treatment pathways and care plans (the "missing pieces") that are preventing people with MS from achieving the treatment outcomes and quality of life goals they desire.

This report reveals survey data taken from specialist healthcare professionals (HCPs) and people with MS based throughout the UK. It outlines recommendations for how the MS community can move towards achieving better outcomes for people with MS.

Missing Pieces Research

The Missing Pieces research was conducted by Adelphi Research UK via two online questionnaires in 2016; one survey for people with MS and one survey for HCPs. Respondents were from England (85%), Scotland (7%), Wales (7%) and Northern Ireland (1%).[8]

The HCP survey was conducted amongst 100 respondents including neurologists, MS specialist neurologists and MS specialist nurses.

It aimed to:

- Evaluate HCP attitudes towards disability associated with MS
- Understand how frequently disability is raised by HCPs with people with MS
- Look at HCP treatment choices, specifically in relation to the importance of disability vs. relapses

The survey of people with MS was conducted amongst 120 people with either RRMS, secondary progressive MS (SPMS), or primary progressive MS (PPMS.) It aimed to:

- Understand people's attitudes towards potential future disabilities and impact on their quality of life
- Capture frequency of discussions about disability at initial diagnosis and in future consultations with HCPs
- Understand concerns at diagnosis vs. current concerns in relation to disability and relapse(s)

*It is important to note that when a person becomes 'disabled' is subjective. The definition of disability is 'a physical or mental condition that limits a person's movements, senses, or activities'; in summary, it is a loss of function and cognition. However, whilst someone with MS may not be able to a do a lot of everyday tasks, they or their families may not consider themselves 'disabled'.

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SECTION 1: ABOUT MS

How MS develops

How MS develops exactly is still unknown, however, it is widely accepted that it is an autoimmune disease where the immune system attacks myelin, the protein that covers the central nervous systems and helps speed up communication between neurons.[9]

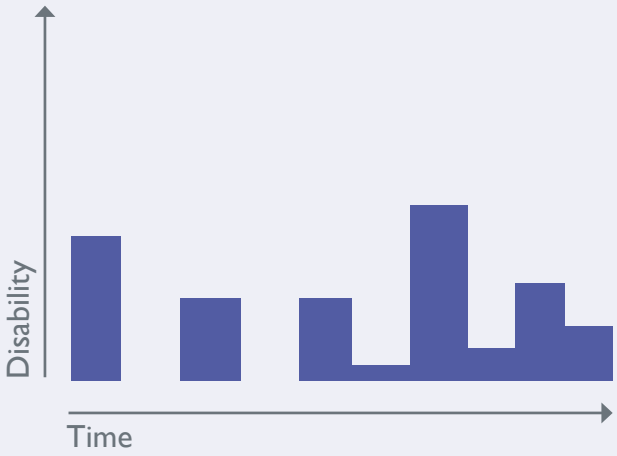
'Sclerosis' means scarring or hardening of tiny patches of tissue, which is caused by relapses or distinct 'attacks' of symptoms. This scarring usually happens in the brain or on the spinal cord. The word 'multiple' is added because this scarring happens at more than one place in the brain and/or spinal cord.

MS is a lifelong condition which can be unpredictable in its course, meaning that the care and treatment pathways for people with MS can vary hugely from person to person and be very complex.

Relapsing Remitting MS (RRMS)

In relapsing remitting MS, people have distinct attacks of symptoms which then fade away either partially or completely.

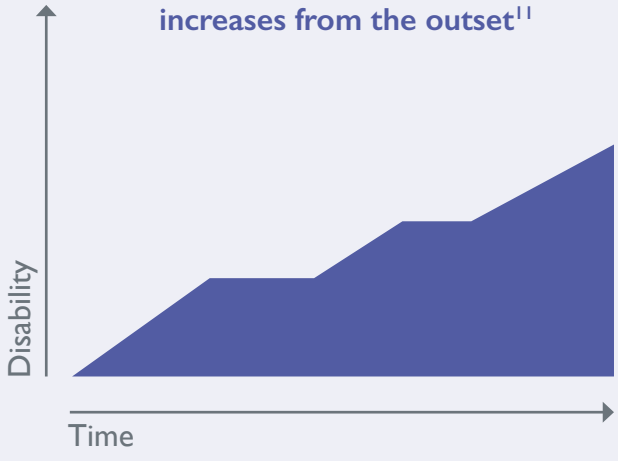
Around 85% of people with MS are diagnosed RRMS



Primary Progressive MS (PPMS)

In PPMS, symptoms gradually get worse over time, rather than appearing as sudden attacks (relapses).

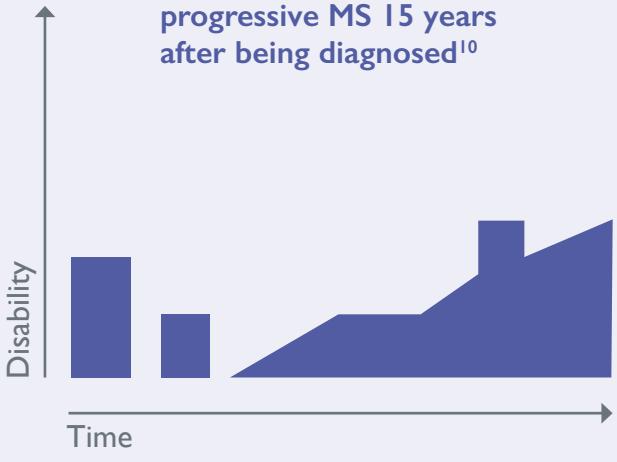
About 10% of people with MS are diagnosed with this form in which disability increases from the outset[11]



Secondary Progressive MS (SPMS)

People originally diagnosed with relapsing remitting MS find that over time the frequency of relapses decreases but disability gradually increases, this is called SPMS.

On average, around 65% of people with RRMS will develop secondary progressive MS 15 years after being diagnosed[10]



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Symptoms of Multiple Sclerosis

Most people with MS are diagnosed in their 20s and 30s and it is the most common condition of the central nervous system affecting young adults.[12]

People who have MS experience a range of symptoms, including fatigue, problems with balance, pins and needles or problems with eyesight. However, the range of symptoms that are associated with MS is vast, meaning that each person's experience is unique.[13]

MS and relapse

MS relapses are a distinct attack of symptoms which then fade away or disappear. Relapses can usually last for more than 24 hours, and up to days or even weeks. **Because of the range of symptoms that people with MS can experience, each relapse can present itself in a different way and can vary from mild to severe.** Many relapses are managed at home with the support of HCPs.

Symptoms and disability

Experiencing symptoms does not necessarily equate to long-term disability in MS. Symptoms that come and go are related to inflammation and damage to the myelin sheath, but progressive long term disability is more linked to nerve loss.

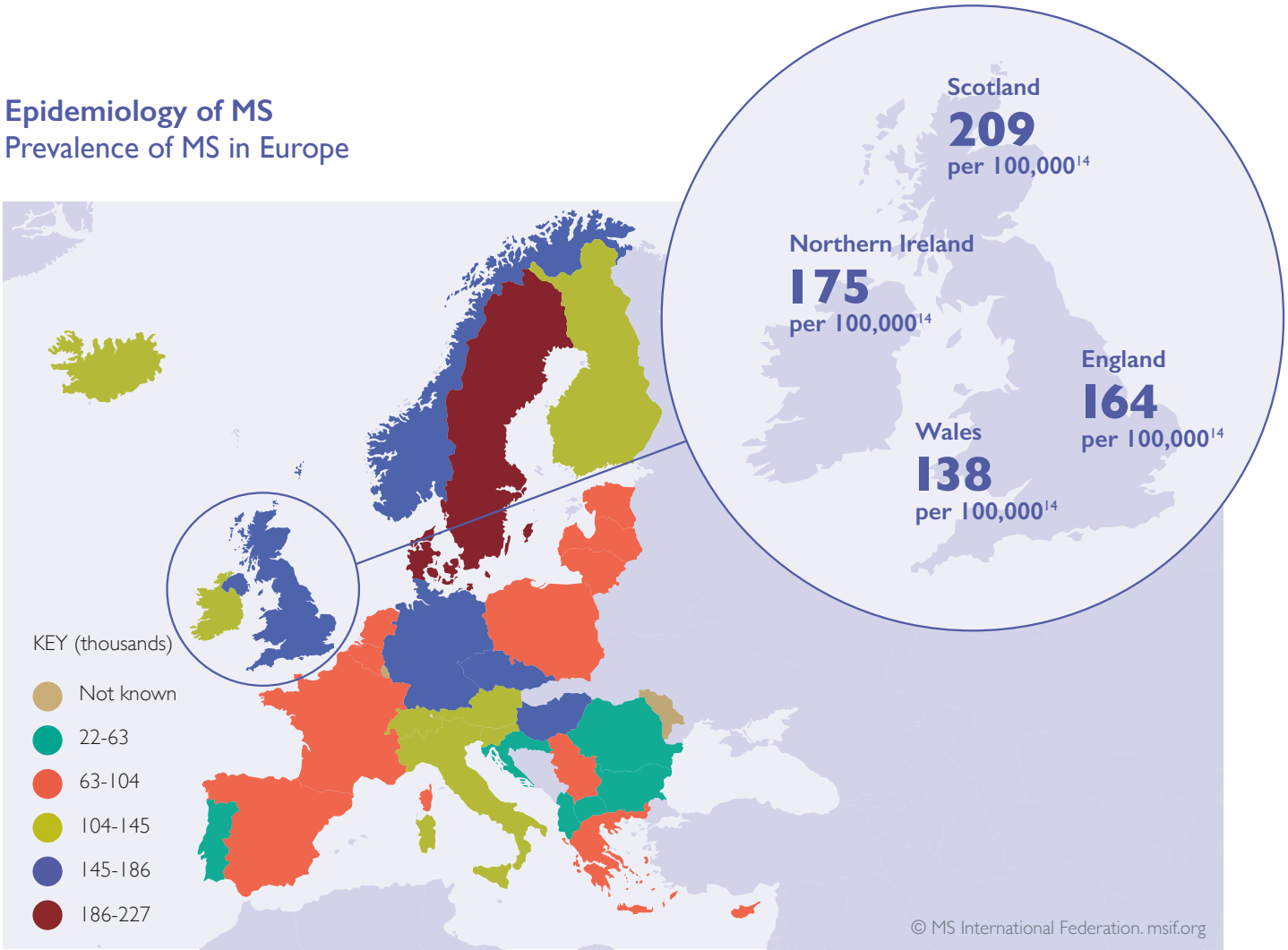
MS prevalence

Over 100,000 people in the UK have MS which represents about one in every 600 people.[14]

However, prevalence rates vary throughout the UK, with **Scotland having the highest rate**.[13]

The current observation is that generally prevalence increases in places further north or south from the equator.[15] The prevalence of MS in the **UK is one of the highest in Europe**, with only **Sweden**, **Hungary** and **Denmark** having higher rates.[14]

Epidemiology of MS
Prevalence of MS in Europe



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SECTION 2: DIAGNOSIS & PROGRESSION

Due to the inconsistent nature of MS symptoms and the number of diagnostic tests involved, MS can take a long time to diagnose. A lot of the individual symptoms can be attributed to other conditions and it tends only to be when a person experiences a number of symptoms simultaneously that they seek medical opinion and testing.

Diagnosis of MS is usually based on clinical judgement by a neurologist with the process including several tests including:

- Magnetic Resonance Imaging (MRI) testing
- Medical or clinical history
- Neurological examination, including checks on movement, coordination, vision, balance, reflexes and other functions of the senses
- Lumbar puncture
- McDonald criteria using MRI evidence to establish evidence of damage to the central nervous system

As MS is a complex disease, each person's experience can require multiple HCPs to help diagnose, assess and input as the disease progresses.

These include MS nurses, occupational therapists, physiotherapists, neuro-rehabilitation consultants, speech and language therapists and neuro-psychologists and sometimes MS specialist neurologists. However, it is the MS nurse and neurologist that play the central roles in this multi-disciplinary team.

The unpredictability of when people with MS might experience relapse, means it can be difficult for people with the condition to access the right treatment and care at the right time. They may need to navigate their way through various different health professionals and healthcare processes/systems.

"It wasn't until a couple of years after my diagnosis that I even knew that there was such a thing as a specialist MS neurologist. This upset me because I'd have liked to have had the choice from the point of diagnosis to transfer to a specialist MS centre if I'd wanted to."

Trishna Bharadia
MS Campaigner and Blogger

"I waited for a diagnosis for about a year then refused treatment initially as my symptoms weren't that bad and I didn't want to be on drugs. I soon changed my mind when my mobility started to suffer."

Abigail Budd
MS Blogger

Managing symptoms, potential relapses, and dealing with complex care and treatment systems can take its toll on people with MS. This is particularly apparent for people with progressive forms of MS, as they are required to deal with even more complex care systems than those with RRMS.[16] Mental health conditions such as depression are commonly experienced by people with MS..[17]

Whilst the severity and frequency of relapses is a focussed on at diagnosis, **the Missing Pieces research found that this did not correspond with the main concern expressed by people with MS — 38% ranked the 'impact of MS symptoms on everyday life' as their biggest concern, versus only 4% that reported relapses as their biggest concern, suggesting they are concerned most with disability**.[8]

For people newly diagnosed with MS, HCPs state that disability is 'routinely discussed' 69% of the time. However, this number contradicts what people with MS report – only 50% recall discussing disability at diagnosis stage.[8]

The main reason HCPs say they did not discuss disability is 'they felt it was not appropriate'. Half of HCPs agree that there is a reluctance to discuss disability with people who have MS, mostly because they do not want to make the person feel uncomfortable.[8] This is especially apparent in MS nurses – the health professional with whom people with MS have the majority of their conversations with.

This general discomfort around discussing the potential onset of disability may be due to the fact that not all people with MS experience the same severity of symptoms – they won't all necessarily experience the worst-case scenario of severe disability and therefore, it is a tricky topic to raise.

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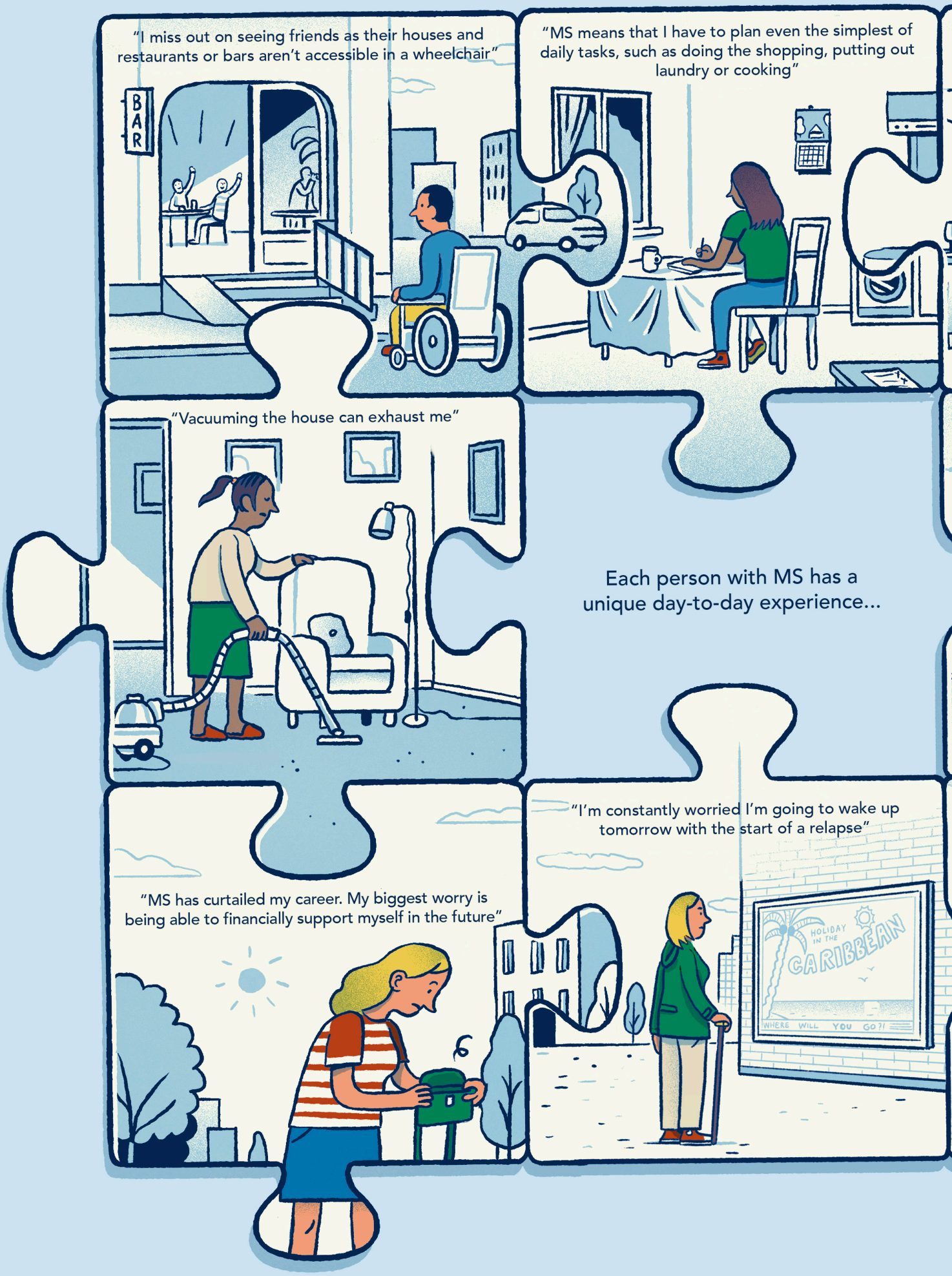
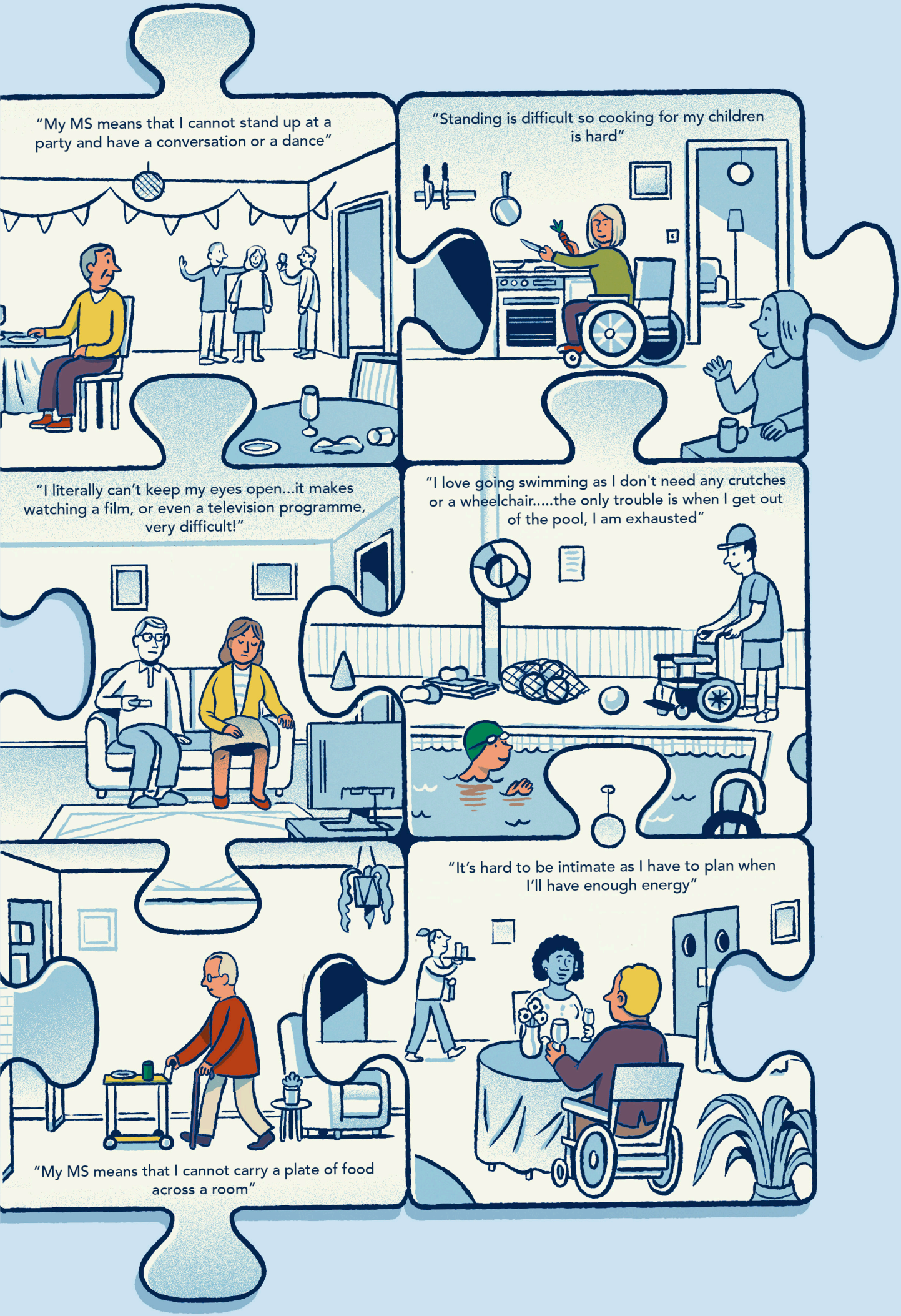
MS: Looking beyond the physical impact




"My MS means that I cannot stand up at a party and have a conversation or a dance"
"Standing is difficult so cooking for my children is hard"
"I literally can't keep my eyes open...it makes watching a film, or even a television programme, very difficult!"
"I love going swimming as I don't need any crutches or a wheelchair.....the only trouble is when I get out of the pool, I am exhausted"
"It's hard to be intimate as I have to plan when I'll have enough energy"
"My MS means that I cannot carry a plate of food across a room"

"Disability to me means both physical and mental symptoms and both visible and hidden symptoms that can have a severe impact on how you can carry out day to day living and tasks."

Trishna Bharadia
MS Campaigner and Blogger

Measuring progression of MS

Monitoring disease progression is an important aspect of ongoing care for people with MS. Currently progression of the disease is measured via MRI scans to see the number of lesions or 'scarring' on the brain, and via physical examination using a disability rating scale – the Expanded Disability Status Scale (EDSS).

The EDSS quantifies disability in eight Functional Systems (FS) and allows neurologists to assign a Functional System Score (FSS) to each of these. Higher numbers reflect a greater degree of disability, mostly in relation to mobility e.g. scores 5-8 out of 10 equates to 'severe disability, impairing your daily activities and requiring assistance with walking'.

HCPs reported that 'impact on independence' and 'ability to work' are considered the main fears and concerns raised by the people they treat, above factors such as 'impact on mobility', which the EDSS mainly focusses on.[8] What this suggests is that people with MS are most worried about not being self-sufficient in the future.

It is important to note that when a person actually becomes 'disabled' is very much subjective. In the UK, the word 'disability' is often linked to government benefits – the point at which a person is in need of these benefits is the point at which they officially call themselves 'disabled'.

Measuring disability

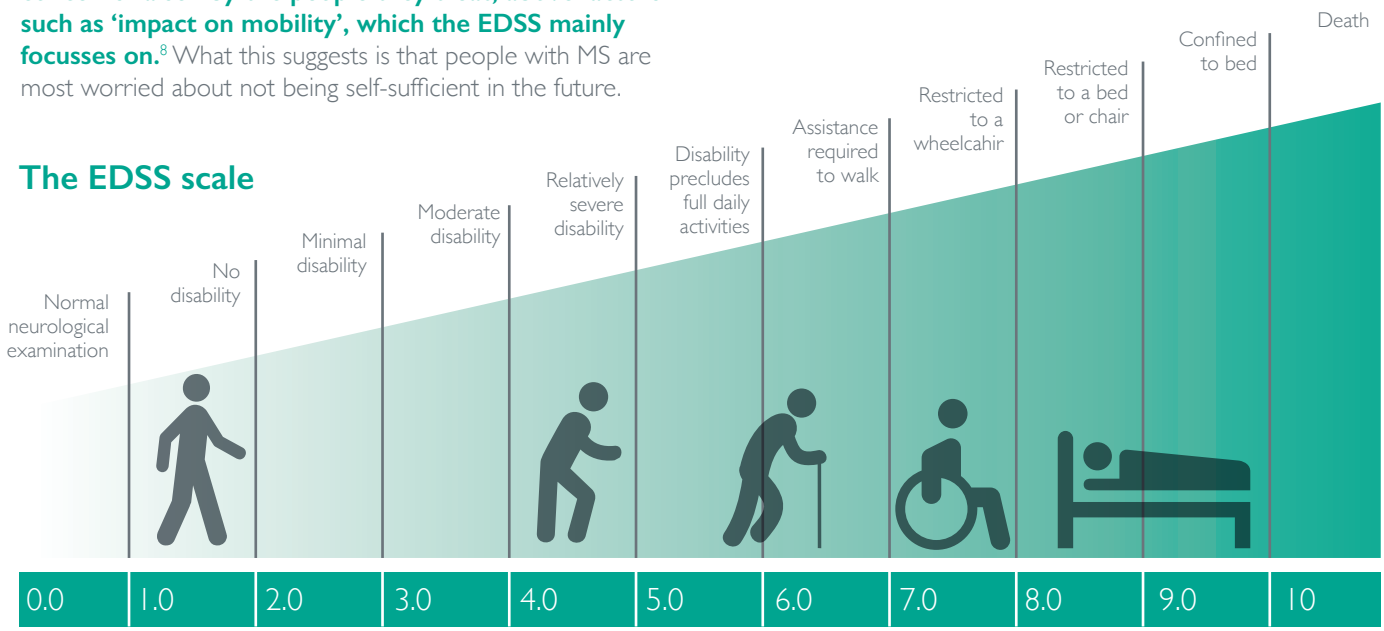
The Expanded Disability Status Scale (EDSS) is the tool currently available and most commonly used by HCPs to quantify disability and monitor progression of the level of disability over time. However, only a quarter of HCPs use it at every consultation.

Both HCPs and people with MS do not necessarily think the EDSS tool measures the full extent of their experiences linked to disability, suggesting it is not fully fit for purpose.

In fact, on average, people with MS gave the EDSS tool a score of 5.6/10 in terms of how well it measures the impact of MS on their day-to-day life.[8]

Many HCPs rely on assessing disability progression simply via 'visual observation'. This is especially true of MS Nurses where 96% state that out of all the ways to assess disability, they use 'visual appearance' the most.[8] This is perhaps due to the fact that nurses see the people they're treating more often than any other HCP in the multi-disciplinary group so are better able to pick up on changes from one visit to the next.

The EDSS scale



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SECTION 3: TREATMENT & ONGOING CARE

The drive for better care

It is recognised by professional bodies, such as the Association of British Neurologists (ABN), that measurement of disease progression and offering treatment as soon as possible is important.[18,19]

The NICE Quality Standards for MS recommend that people with MS have access to care from a multidisciplinary team with expertise in MS and access to a comprehensive review of their treatment and care annually.[20] The *MS Forward View: A Consensus on the Future of MS Services*, published by the MS Trust in November 2016, also stated that 'MS teams should offer everyone with MS a comprehensive annual review with an appropriate health professional who has specialist expertise in MS'.[21]

Despite these recommendations it is reported that 36% of people with MS had not seen a neurologist in the past 12 months and overall one in ten said they'd not seen a neurologist recently but felt they needed to.[1]

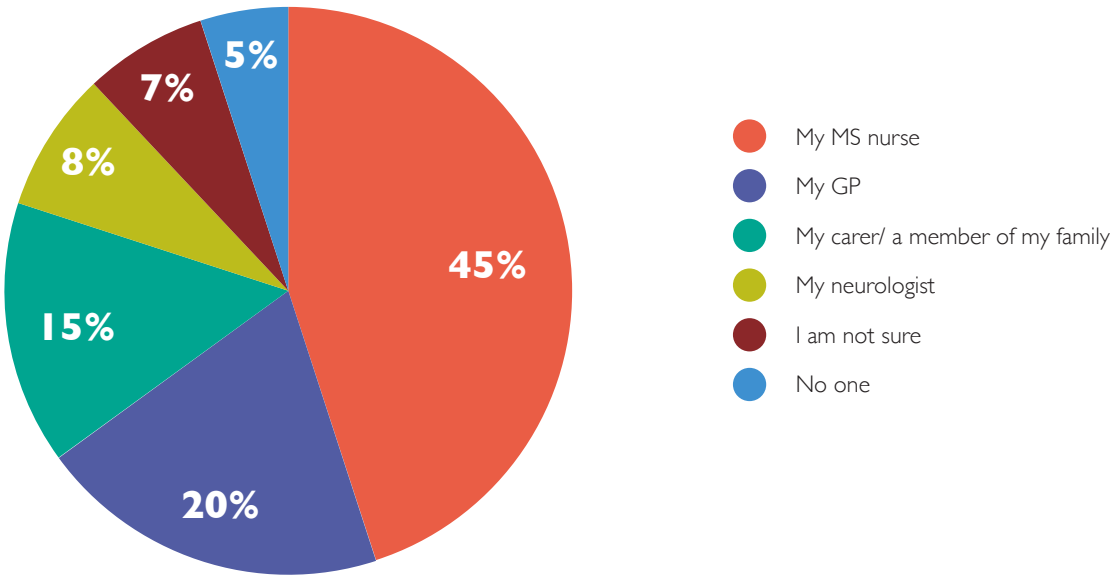
While people with MS are in contact with a multidisciplinary team, identifying or accessing the right healthcare professional to help them with their treatment decisions may be challenging. The most common key contact for healthcare and support in relation to MS is a specialist nurse but it is the MS specialist neurologist that would initiate, for example, a DMT treatment.[8]

The new NICE Quality Standards in MS[19], published in 2016, set out the level of services expected and recommend that people with MS:

- Are given support at the time of diagnosis to understand the condition, its progression and the ways it can be managed by the consultant neurologist making the diagnosis.
- Are offered a face to face follow-up appointment with a HCP with expertise in MS, to take place within six weeks of diagnosis.
- Have a single point of contact who co-ordinates access to care from a multidisciplinary team with expertise in MS.
- Are offered support to remain physically active if they have problems with mobility or fatigue
- Are offered treatment as soon as possible and within 14 days of the onset of symptoms, if they have had a relapse
- Are offered a comprehensive review at least once a year by HCPs with expertise in MS.

The NHS Quality Improvement Scotland published national standards of care for neurological conditions in October 2009. The local Department for Health, Social Services and Personal Safety Northern Ireland considers NICE Guidance, and any endorsements are published on its website.[22]

Key contact for healthcare and support[1]



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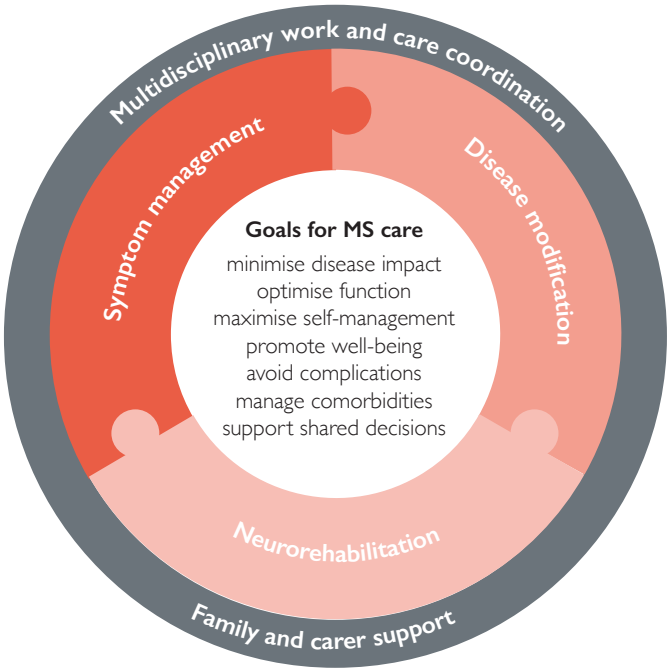
A holistic model for MS care[21]



Access to recent MS treatment advances

Since becoming available, DMTs have changed the RRMS treatment landscape. They can reduce the number of relapses as well as reduce the severity of relapses, and some can also slow down disease progression and disability. There are 11 drugs approved for use by the NHS in the UK.

It is important to note that in the UK, DMTs are only prescribed to those with RRMS or secondary progressive MS who meet certain criteria.

The My MS, My Needs Surveys by the MS Society[1,2,3,4] focussed on access to treatment in the UK and revealed big disparities in the services offered from one part of the country to another.

Recently, a follow-up survey involving 11,024 people with MS across the UK (one of the biggest MS surveys ever) showed that over the last three years, access to DMTs in England among those who could benefit has increased. However, the UK still has one of the worst rates of DMT use in Europe, with regards to people with MS receiving a DMT.[23,5]

With more choice of DMTs becoming available, it is now more important than ever that people are able to talk to an MS specialist as soon as possible after diagnosis about the treatment option that would best suit them.

Disability and treatments

As well as difficulty in prompt access to treatment, many people with MS are still not receiving advice about delaying disability from their HCP. Many people naturally learn about relapses when they are diagnosed but not about potential disability. **When asked, two thirds (65%) of people with MS say maintaining independence is their main treatment goal, followed by reducing relapses. However 22% of people with MS say the HCP they see does not discuss treatment goals with them.**[8]

There is also a lack of clarity and information surrounding MS. **Over a quarter of people with MS (28%) are not aware that the number of relapses in MS (that measures worsening of MS) is not directly linked to disability progression (e.g. difficulty working or performing everyday tasks such as walking, concentrating, etc.). When aware of this, 66% saw delaying disability as a more important treatment goal than reducing the frequency of relapses.** Additionally, 24% of people with MS are not aware that treatments help to delay disability.[8]

Those who do not have adequate access to the right care may be missing out on treatments that could put off disability, allowing for a more fulfilled life for longer. **Around three quarters of HCPs think people with MS face delays in being initiated onto a DMT in particular, with the main reason being limited access to MS specialist neurologists.**[8] This means that even if people with MS do have treatment goals, the care system in the UK does not necessarily allow them to be met. **The NHS Five Year Forward View highlights that ill-health prevention is a key priority to making the NHS more sustainable, and early access to MS specialist neurologists and treatments are something that could contribute to this sustainability.**[23]

In order to ensure no-one with MS misses out and everyone is given the best chance to live their life independently for as long as possible, we need to move from the current 'watch and wait' system where people with MS are advised to see whether more relapses occur before making a decision on treatment plans to a more proactive preventative care model. **Each person must have an individualised care plan with their treatment goals as the focus.**

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SECTION 4: WHAT HAPPENS NEXT?

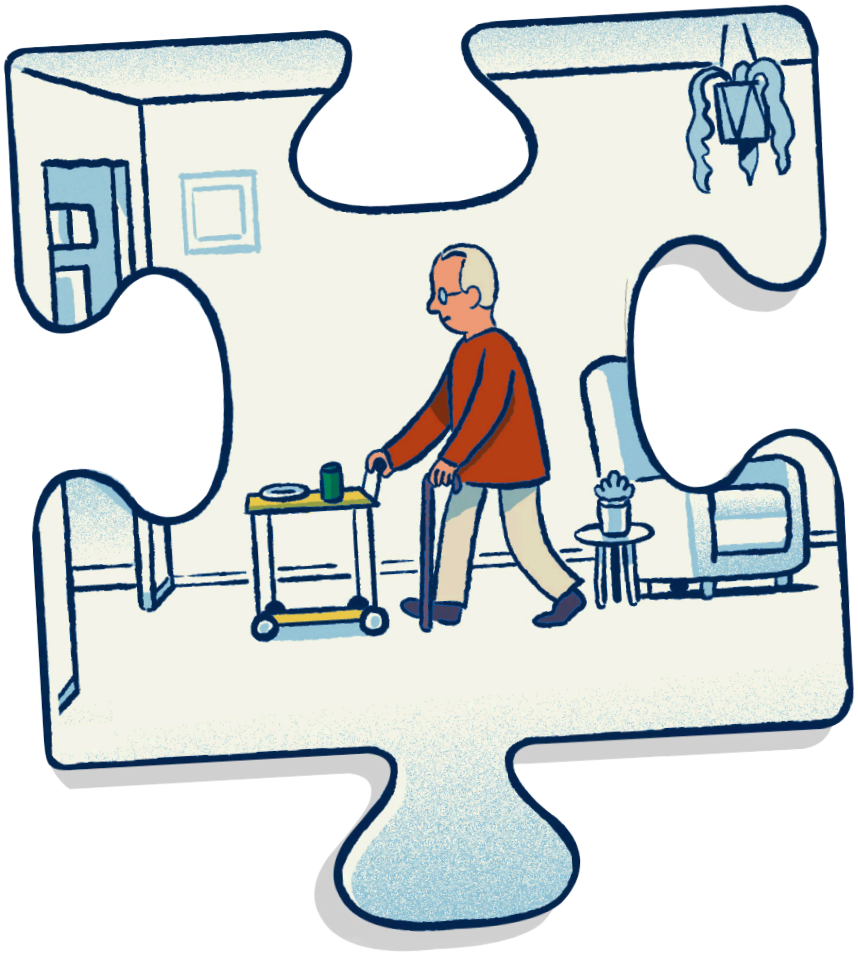
With the arrival of DMTs, people with MS are becoming more aware of monitoring their own condition and want to be involved in their treatment decisions. **In fact, 40% of discussions about disability are actually initiated by the person with MS. But a large proportion (42%) would prefer to discuss disability more frequently with their HCPs.**[8] These ongoing conversations will help empower and reassure people with MS that the likelihood of disability progression is being tracked and managed. This is linked to the importance of holistic annual reviews by an MS specialist, as NICE recommends,[6] and also further care planning resulting from these reviews.

It is clear that disability is an important concern for people with MS, over half (54%) of people with MS said they are worried and 45% said they were scared at the prospect of becoming disabled.[8]

There needs to be more support for both people with MS and carers on the emotional burden that the uncertainty of MS can bring.

Summary key points:

- People with MS are concerned about disability but that concern may not be addressed during the consultation with their HCPs
- Modern therapies, particularly DMTs, can play a critical role in delaying the onset of disability allowing people with MS to continue to live full and productive lives
- It has been shown that the UK is failing to make these therapies available to people that need them. This means there is a danger of the NHS not being able to prevent people with MS becoming more sick in the long term and therefore risking putting further strain on NHS finances.



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SECTION 5: LOOKING TO THE FUTURE

Sanofi is committed to working with the whole of the MS community to ensure that every person in the UK with MS receives a standard of care that, at a minimum, matches that delivered in other major European countries such as Germany, France, Spain and Italy. We know that there are missing pieces in both the conversations people are having with their healthcare professionals and in the care plans and treatments they are receiving – we are committed to support those to be filled in. And we will focus on ensuring that the care delivered to people with MS is centred around the things that matter most to them.

This includes:

TODAY

01

Being able to understand the diagnosis, prognosis and care pathway

Understanding what type of MS has been diagnosed, how 'active' it is, what symptoms may be experienced and what impact this may have both now and in the longer term on both physical and mental ability.

THE AMBITION:

Every person with MS should be offered a follow-up face to face appointment six weeks after diagnosis with a HCP with expertise in MS, as per the NICE Quality Standards for MS.[6] They should also be talked through, or directed towards sources of information on the care pathway, in order to understand who may be involved, at what point, and what mandates are in place that govern their care.

02

Knowing their treatment options and being able to express their treatment goals

Every person with MS should have knowledge and understanding of the different treatment options available to them and be given the opportunity to express what their personal goals are for treatment – this should inform shared-decision making.

THE AMBITION:

At an appointment six weeks post diagnosis, every person with MS should be encouraged to express their treatment goals and jointly agree a treatment plan with their current situation.

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03
Starting on DMTs as quickly as possible

Every person with MS should have prompt access to treatments that can change the course of their disease (DMTs).

THE AMBITION:

Every person with MS should have access to DMTs from diagnosis, or at minimum within 14 days of the onset of symptoms if they have experienced a relapse (in line with the NICE Quality Standards for MS).[20]

04
Having access to a multidisciplinary team who can deliver integrated care centered around the individual

People with MS should have prompt and simplified access to a multidisciplinary team that can provide the three key pillars of MS care: symptom management; disease modification; and neurorehabilitation[21]. Care should be centred around the needs of the individual with MS, as opposed to being centered around organisational structures[21].

THE AMBITION:

Every person with MS should have a single point of contact, in line with the NICE Quality Standards for MS, who can effectively coordinate their care.

05
Having an individualised care plan and regular reviews

MS is a heterogeneous disease therefore every person with MS needs an individualised approach to their disease management. With MS being a progressive and lifelong disease, regular reviews of the care plan are essential to ensure they are delivering in line with changing needs.

THE AMBITION:

Every person with MS has an individual care and treatment plan in place, which is discussed and reviewed at least once a year with a HCP with a specialism in MS, in line with the NICE Quality Standards for MS.[8]

FUTURE

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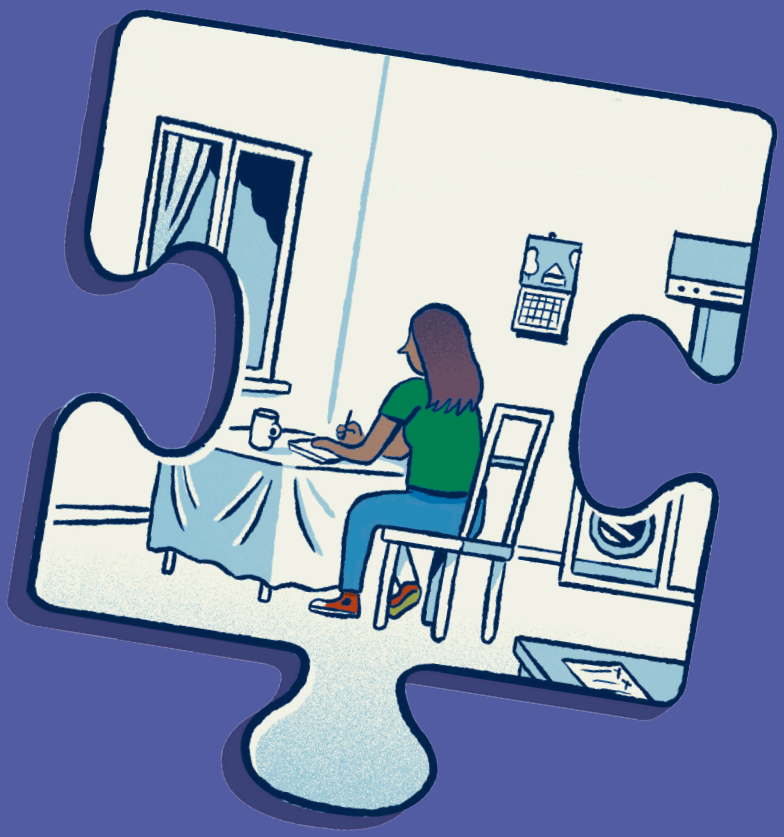

REFERENCES

1 MS Society. MS treatment in England. Available at: *https://www.mssociety.org.uk/sites/default/files/MS%20treatment%20in%20England_0.pdf*. Accessed February 2017.

2 MS Society. MS treatment in Wales: is access still a lottery? Available at: *https://www.mssociety.org.uk/sites/default/files/MS%20treatment%20in%20Wales%20WALES%20FINAL.pdf*. Accessed February 2017.

3 MS Society. MS treatment in Scotland: is access still a lottery? Available at: *https://www.yumpu.com/en/document/view/55847146/ms-treatment-in-scotland-is-access-still-a-lottery*. Accessed February 2017.

4 MS Society - MS treatment in Northern Ireland: is access still a lottery? Available at: *https://www.mssociety.org.uk/sites/default/files/MS%20treatment%20in%20Northern%20Ireland.pdf*. Accessed February 2017.

5 European Multiple Sclerosis Platform. Multiple Sclerosis in Europe. Available at: *http://www.emsp.org/wp-content/uploads/2015/08/MS-in-EU-access.pdf*. Accessed February 2017.

6 National Institute of Clinical Guidance. Multiple Sclerosis. Available at: *https://www.nice.org.uk/guidance/QS108/chapter/List-of-quality-statements*. Accessed February 2017.

7 Sanofi data on file, May 2016.

8 Sanofi data on file, March 2017.

9 MS Trust. Causes of MS. Available at: *https://www.mstrust.org.uk/a-z/causes-ms*. Accessed February 2017.

10 MS Society – Types of MS. Secondary Progressive. Available at: *https://www.mssociety.org.uk/what-is-ms/types-of-ms/secondary-progressive-spms*. Accessed April 2017.

11 MS Trust. Types of MS. Available at: *https://www.mstrust.org.uk/a-z/types-ms*. Accessed February 2017.

12 MS Trust. Introduction to MS. Available at: *https://www.mstrust.org.uk/understanding-ms/what-ms/introduction-ms*. Accessed February 2017.

13 MS Trust. Symptoms. Available at: *https://www.mstrust.org.uk/a-z/symptoms*. Accessed February 2017.

14 MS Society. MS in the UK. Available at: *https://www.mssociety.org.uk/sites/default/files/MS%20in%20the%20UK%20January%202016_0.pdf*. Accessed February 2017.

15 MS International Federation. Atlas of MS. Available at: *https://www.msif.org/about-us/advocacy/atlas/?gclid=CNSfuM-G7NACFc-_7QodCiEMow*. Accessed February 2017.

16 MS Trust. Evidence for MS Specialist Services: Findings from the GEMSS MS specialist nurse evaluation project. Available at: *https://support.mstrust.org.uk/file/Evidence-for-MS-Specialist-Services.pdf*. Accessed February 2017.

17 Feinstein, A *et al*. The link between multiple sclerosis and depression. Nat *Rev Neurol*. 2014 Sep;10(9):507-17. doi: 10.1038/nrneurol.2014.139.

18 Giovannoni G, *et al*. Time matters in multiple sclerosis – international consensus recommendations on diagnosis, management and access to treatment. *Mult Scler Relat Disord*. 2016; 9 Suppl 1:S5-S48. doi: 10.1016/j.msard.2016.07.003. Epub 2016 Jul 7.

19 Solding N, *et al*. Association of British Neurologists: revised (2015) guidelines for prescribing disease-modifying treatments in multiple sclerosis. Available at: *http://pn.bmj.com/content/early/2015/06/20/practneurol-2015-001139.full*. Accessed February 2017.

20 National Institute of Clinical Guidance. Multiple Sclerosis. Available at: *https://www.nice.org.uk/guidance/QS108/chapter/List-of-quality-statements*. Accessed February 2017.

21 MS Trust. MS Forward View: a consensus for the future of MS services November 2016. Available at: *https://www.mstrust.org.uk/sites/default/files/Future%20of%20MS%20Services%20WEB%20FINAL.pdf*. Accessed February 2017.

22 MS Society. A NICE new Quality Standard for care. Available at: *https://www.mssociety.org.uk/get-involved/campaigns/campaigns-blog/2016/01/nice-new-quality-standard-care*. Accessed February 2017.

23 National Health Service. NHS Five Year Forward View October 2014. Available at: *https://www.england.nhs.uk/wp-content/uploads/2014/10/5yfv-web.pdf*. Accessed February 2017.

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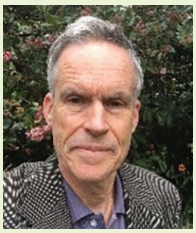
Dr Michael Hayes



is a Consultant Neurologist and Head of Neurology at Concord hospital with an interest in movement and functional disorders.

Juliet M Smith

BA, DipAud, is a Clinical Audiologist who graduated at Macquarie University in 1988 and has trained and practiced clinical audiology at the National Acoustic Laboratories in London in addition to experience at St Vincent's & Concord Hospitals and in private ENT clinics in Sydney. She has had over 25 years experience in this field and continues to provide diagnostic services for adults and children with a special interest in tinnitus management through Concord Hospital and also as a secondary referral service to audiologists throughout NSW.

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Adult onset unilateral functional hearing loss:
a case report and discussion

Key Points

- Functional hearing loss is a rare manifestation of non-organic illness in adults
- Unlike other non-organic illnesses, functional hearing loss is readily amenable to objective diagnosis
- The auditory axis can be interrogated via audiological and electrophysiological investigations from the level of the tympanic membrane to the auditory cortex

Abstract

Unilateral functional or non-organic hearing loss is a rare condition in adulthood which unlike many other functional diseases in neurology can be relatively easily identified with simple audiological assessment and investigations that target distinct parts of the auditory pathway. We describe a previously healthy 19-year-old female who presented with an acute onset of unilateral non-organic hearing loss with ipsilateral visual and sensory symptoms. We briefly review the literature on functional hearing loss and some of the tests available to investigate it.

Case study

A 19-year-old female presented to an emergency department with an acute onset of right sided hearing loss, mild right eye visual blurring and numbness affecting the right arm and leg.

Nine months earlier she had developed right sided ear pain with discharge diagnosed as otitis externa by an ENT specialist and treated successfully. Six weeks later, she had two further episodes of right sided tinnitus and progressive step-wise deterioration of her hearing with audiometry performed on two successive tests over 5 months yielding pure-tone averages of 48 and 51 dB HL on the right ear and 21dB and 16 dB HL on the left (normal threshold ~10-15 dB HL). These symptoms were accompanied by right mastoid process tenderness. She was diagnosed as having unilateral idiopathic sensorineural hearing loss and was treated with courses of oral steroids without benefit.

Examination in the emergency department revealed hearing loss in the right ear on bedside examination, slightly decreased visual acuity to 6/9 in the right eye and reduced pinprick and light touch sensation over the right arm and leg but not the face. Ophthalmological review revealed a normal cornea, lens, retina and visual fields with no evidence of interstitial keratitis to suggest Cogan's syndrome. Inflammatory markers including ESR, CRP, ANA, ENA and ANCA were negative and an MRI of the brain was normal, with no evidence of abnormalities in the internal acoustic meati and the mastoid cavities.

Initial pure-tone audiometry demonstrated a normal hearing threshold for the left ear (pure tone average = 15dB HL) and severe hearing loss on the right (pure tone average = 85 dB HL). She was initially treated with a short course of oral prednisone for possible recurrent idiopathic sensorineural hearing loss (SNHL).

Subsequent assessment indicated that her speech audiometry for the right ear was better than that expected from her pure tone testing with a recognition score of 67% at 30 dB. Unmasked audiometry did not reveal the expected "shadow curve" on right ear testing representing transmission of auditory stimuli to the intact left ear and reported hearing thresholds showed poor reproducibility. A Stenger test was positive, indicating a non-organic pattern of hearing loss. While our patient's reported auditory threshold on her right ear was in the range of 80 dB, Stenger testing at octave frequencies between 250-8000 Hz yielded true thresholds between 10 – 20dB (Table 1).

Transient and distortion product otoacoustic emissions (TEOAEs and DPOAEs, respectively) were clearly present indicating intact cochlear outer hair cell function. Brainstem auditory evoked responses (BAER) using stimuli above and below reported thresholds (75 & 92 dB nHL) were normal bilaterally confirming the intact

Table 1: Stenger Test Thresholds							
		Stimulus Frequency					
		250Hz	500Hz	1000Hz	2000Hz	4000Hz	8000Hz
Left Ear Stimulus (dB)		15	10	15	20	10	10
		Response to right ear stimulus					
Right Ear Stimulus (dB)	40	NR	NR	NR	NR	NR	NR
	30	NR	NR	NR	NR	NR	NR
	25	NR	NR	NR	NR	NR	NR
	20	NR	NR	R	NR	NR	R
	15	R	NR		R	R	
	10		R				
Key: NR = No Response R = Response							

pathways from the auditory nerve to the inferior colliculus. Cortical evoked potentials recorded using 1000 Hz and 4000 Hz stimuli of 0 – 80 dB nHL at 10 dB intervals yielded thresholds of 20 dB nHL on either side, indicating symmetrical and normal or very near normal hearing at the tested frequencies (Figure 1 below).

Her right-sided visual and sensory symptoms resolved over a few days but she reported persistent hearing loss as well as episodic true spinning vertigo lasting seconds on review one month later. She was referred to a neuro-otologist for further investigation of her auditory and vestibular function.

Neuro-otological assessment revealed no spontaneous, gaze-evoked, head-shaking or positional nystagmus. Bedside and 3D video head impulses in all six semicircular canal planes were normal, as were ocular and cervical vestibular evoked myogenic potentials, indicating that all five vestibular end organs were intact. Although plans were made for the patient to record video-oculography at home to capture nystagmus accompanying her episodic vertigo, the episodes ceased after this assessment.

Further evaluation revealed recent psychological stressors including a relationship breakdown, parental pressures and recent deferment of her tertiary studies. The patient was reassured that investigations had revealed her auditory pathways were intact; non-organic hearing loss was discussed.

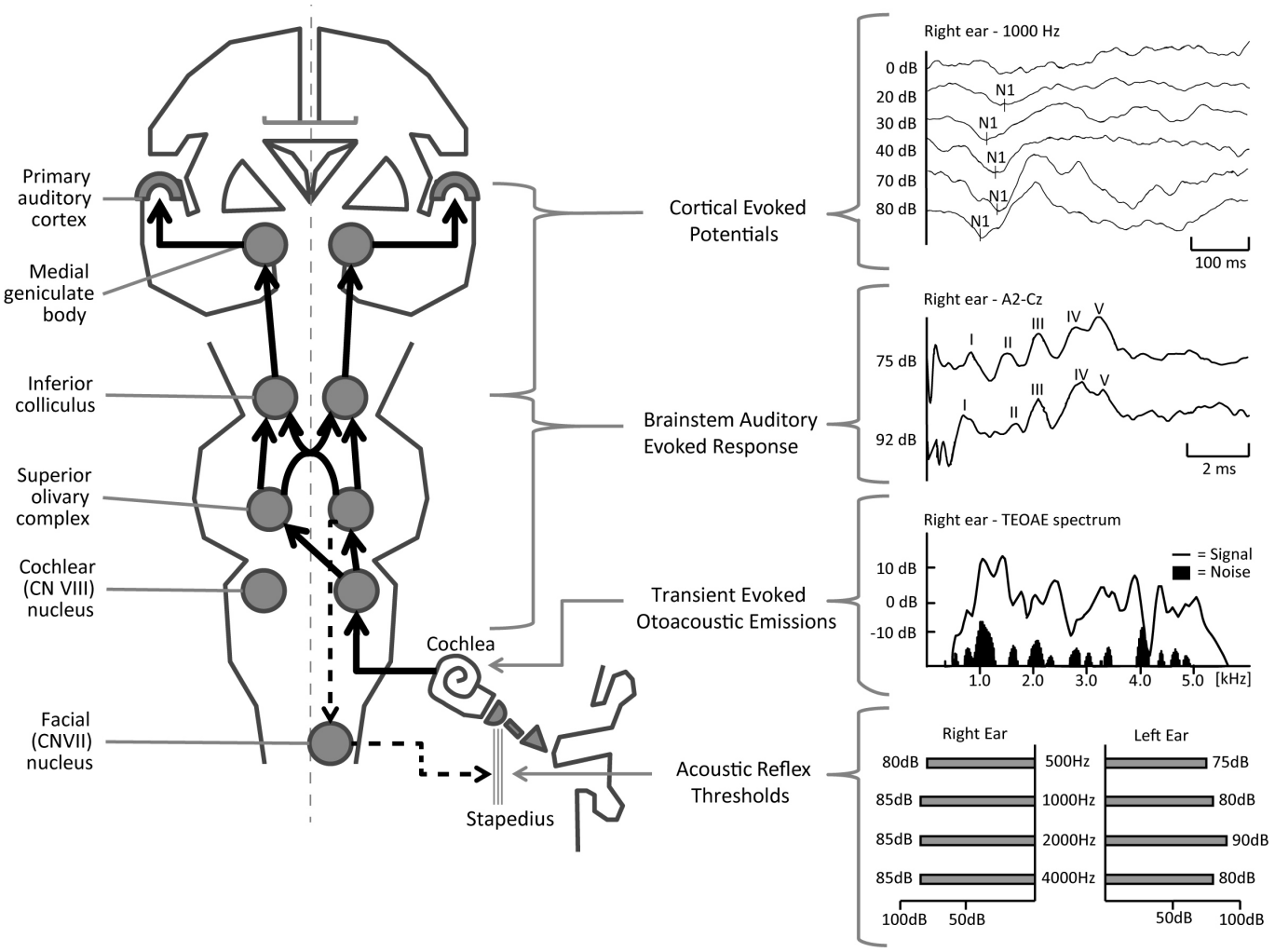

Figure 1: Objective testing of the auditory axis and results in our patient

Sound waves are conducted by the ear through the ossicular chain to the cochlea where the hair cells transduce the signal into a neural impulse that is transmitted along the cochlear part of cranial nerve VIII to the ipsilateral cochlear nuclei. Auditory signals are relayed through to bilateral superior olivary complexes and rostrally through the inferior colliculi and medial geniculate bodies before connecting with the primary auditory cortex on the superior temporal gyrus bilaterally.

Objective tests of this axis include cortical evoked potentials that correspond with responses arising from the inferior colliculus through to the cortex. The brainstem auditory evoked response has numbered waveforms that correspond with structures from the cochlear nerve to the inferior colliculus. Otoacoustic emissions are mediated by the cochlear outer hair cells in response to auditory stimuli and can be detected in the external ear canal. Finally the acoustic reflex is triggered by suprathreshold auditory stimuli and is mediated by efferents originating from the superior olivary complex and synapsing with the facial nuclei causing contraction of the stapedius muscle and tautening of the ossicular chain which is detectable through impedance testing. Representative normal results from our patient are shown on the right side of the figure.

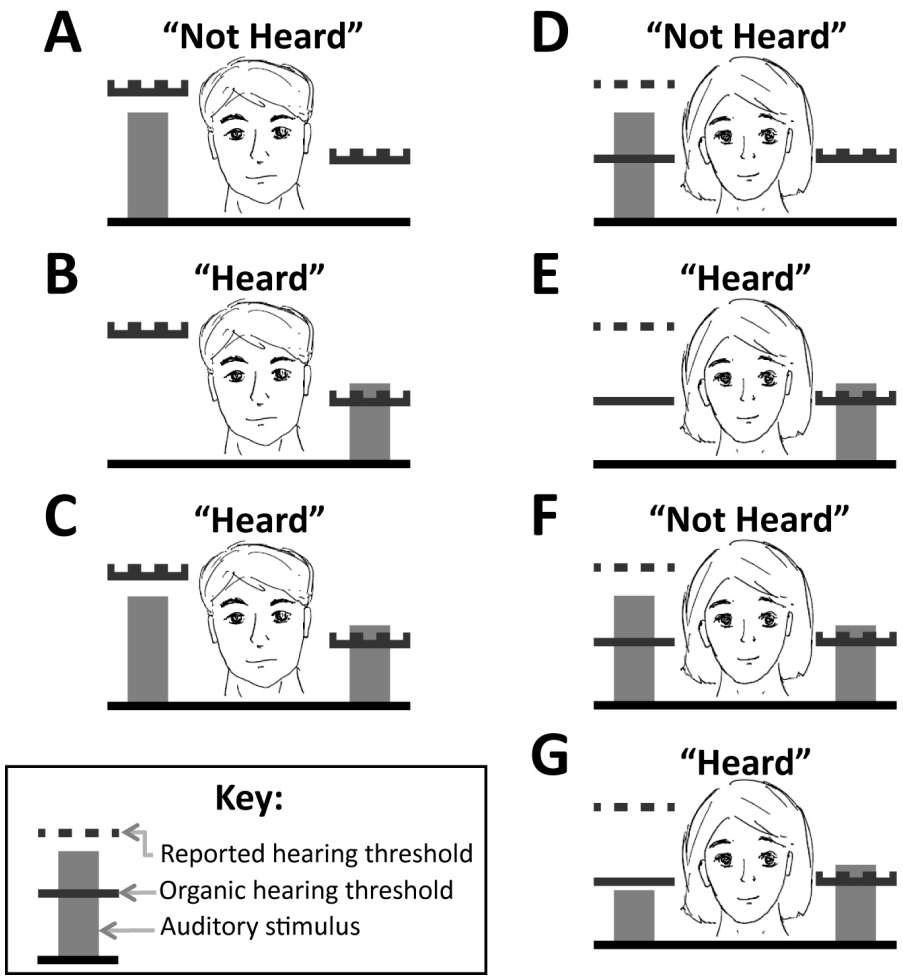

Figure 2: The Stenger test in differentiating organic and non-organic unilateral hearing loss

The Stenger test can be used to differentiate organic and non-organic causes of unilateral hearing loss through exploiting the binaural fusion phenomena by which a tone of the same frequency displayed to both ears simultaneously is perceived only in the ear in which it is louder.

True auditory thresholds are represented in this diagram by solid lines for each ear. Reported auditory thresholds or the level above which sound is reported as heard is represented by dotted lines. Auditory stimuli presented to each ear are displayed as vertical bars, the height of which corresponds to the intensity of the stimulus.

Consider panels (A)-(C) representing a patient with an organic cause of right sided deafness, seen as high auditory thresholds on the right. In panel (A), a subthreshold stimulus presented to the right ear is not heard whereas a suprathreshold left stimulus in (B) is heard. In panel (C) with both stimuli presented together, the subject perceives the suprathreshold left tone and gives a response of "heard", a plausible physiological result.

Consider panels (D)-(G), representing our case, of a patient with non-organic right sided deafness and an elevated reported auditory threshold but normal organic threshold on the right. When presented in isolation, the "sub threshold" right stimulus is reported as "not heard" in (D) and the supra threshold left stimulus is heard in (E). However when these two tones are presented together in (F), the subject perceives the louder tone only on the right by virtue of fusion phenomena and gives a "not-heard" response. This result is implausible and non-physiological given that the same tone played to the left ear alone in (E) is reported as heard, strongly suggesting a non-organic hearing loss. When a tone below the subject's true right threshold is combined with the supra threshold left stimulus in (G), the subject then lateralises to the intact left ear and provides a "heard" response.

Whilst accepting this diagnosis, she continued to report ongoing hearing impairment. Ten months later she presented to another hospital with an acute left hemi-paresis which resolved spontaneously within two days and for which no organic cause could be found. Upon follow-up at the time of manuscript preparation, the patient agreed to see a clinical psychologist in order to further address her non-organic symptoms.

Discussion

Non-organic presentations are common in neurology and can be diagnostically challenging. In such cases, the role of the Neurologist is primarily to exclude organic disease which is attempted by a combination of thorough clinical evaluation and appropriate investigations.[1] This case of adult-onset unilateral non-organic hearing loss highlights an uncommon presentation which is particularly amenable to diagnosis via audiological testing.

Functional hearing loss is more common in children and is rare in adults outside of military populations where considerations of financial compensation may skew results.[2] In adults, it typically presents in 20-40 year olds with a female predominance, differentiating it from idiopathic SNHL which typically affects those beyond the 5th decade of life.[3] In one Japanese case series, 24 of 31 patients were female with an age range between 7 and 39 years. Approximately 45% of these patients presented with unilateral hearing loss, 45% with bilateral loss and the remainder with a mix of organic and non-organic disease in different ears.[3]

In the majority of non-organic hearing loss, the diagnosis can be made by audiological techniques alone. Hallmarks of non-organic disease on audiological testing as shown in our case include inconsistencies in thresholds on repeat testing (>10dB), and speech recognition thresholds that are markedly superior to pure tone audiometric thresholds.[4,5] A 'shadow curve' is the level at which an air conducted stimulus may be heard by the contralateral normal ear in unilateral deafness.[5] The absence of a 'shadow curve' as evident in our case is a marker of non-organic hearing loss.

The Stenger test (Figure 2) has been in existence for more than 100 years and has good sensitivity (99%) and moderate specificity (~70%) in the evaluation of unilateral non-organic hearing loss.[6] Measurement of the stapedial reflex via impedance testing is another technique to confirm the intact function of the auditory nerve, lower auditory brainstem pathways, the middle and inner ear. This response consists of the contraction of the stapedius muscle in response to an auditory stimulus above threshold and can be detected in the compliance of the tympanic membrane[5] – our patient's stapedial reflexes were normal bilaterally (Figure 1).

OAE is a method employing the ability of the outer hair cells of the cochlea to generate low frequency sounds detectable within the external acoustic canal in response to auditory stimuli. They are typically present only when true hearing thresholds are ≤20dB HL[7] and have been described by some authors specifically in the evaluation of functional hearing loss.[8] Both TEOAEs and DPOAEs were measured and present bilaterally in our patient.

The BAER is an averaged electrical response detectable from surface electrodes originating from the cochlear nerve and brainstem. BAERs have been used to infer true auditory thresholds by other authors.[9] BAERs were normal in morphology and latencies bilaterally in our patient.

Non-organic hearing loss is not always a self-limiting disorder. In a case series of six adult patients with proven unilateral non-organic hearing loss for instance, only two cases had resolved twelve months after onset despite knowledge of the diagnosis.[10]

We thus describe an unusual case of non-organic illness presenting as an acute onset of unilateral hearing loss. It is possible that the initial episode of otitis externa served as a model for her subsequent presentation. Unlike many other non-organic illnesses in neurology, functional hearing loss is readily diagnosable via audiological techniques that include perceptual tests, objective threshold testing and tests that assess specific parts of the auditory pathways.

Authorship Statement

J Lee was involved in the initial care and assessment of the patient. He researched, drafted and reviewed the manuscript and also created and compiled the associated figures.

J Smith was involved in the audiological assessment of the patient. She participated in the drafting and reviewing of the manuscript.

R Taylor was involved in the audiological assessment of the patient and in reviewing the manuscript and figures.

M Welgampola was involved in the care and assessment of the patient. She drafted and reviewed the manuscript and figures and also provided scientific direction and guidance.

M Hayes was involved in the care and assessment of the patient. He drafted and reviewed the manuscript and figures and also provided scientific direction and guidance.

Patient consent

The patient has provided informed written consent for the publication of her clinical history and investigations in the medical literature.

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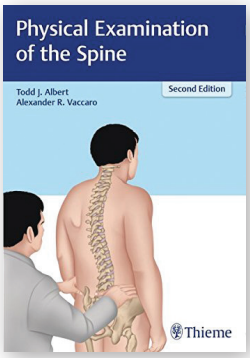
REFERENCES

1. Hayes M, Thompson PD. Chapter 39: Psychogenic movement disorders. In Hallett M. *Movement Disorders, Handbook of Clinical Neurophysiology*, Volume 1.: Elsevier; 2003;p629-638.
2. Austen S, Lynch C. *Non-organic hearing loss redefined: understanding, categorizing and managing non-organic behaviour.* Int J Audiol. 2004;p.43(8):449-457.
3. Hiraumi H, Tsuji J, Kanemaru SI, et al. *Non-organic hearing loss.* Acta Otolaryngol Suppl. 2007;(557):3-7.
4. Lin J, Staecker H. *Nonorganic hearing loss.* Semin Neurol. 2006;p. 26(3),321-330.
5. Gelfand SA. *Nonorganic hearing loss.* In Gelfand SA. Essentials of Audiology, 3rd Edition. New York: Thieme Medical Publishers; 2009;p.404-424.
6. Durmaz A, Karahatay S, Satar B, et al. *Efficiency of Stenger test in confirming profound unilateral pseudohypacusis.* J Laryngol Otol. 2009;p.123(8):840-844.
7. Gorga MP, Neely ST, Berman BM, et al. *A Comparison of transient-evoked and distortion product emissions in normal-hearing and hearing-impaired subjects.* J Acoust Soc Am. 1993;p.94(5):2639-2648.
8. Balatsouras DG, Kaberos A, Korres S, et al. *Detection of Pseudohypacusis: A Prospective Randomized Study of the use of Otoacoustic Emissions.* Ear Hear. 2003;p.24(6):518-527.
9. Sanders JW, Lazenby BB. *Auditory brain stem response in the assessment of pseudohypacusis.* Am J Otol. 1983;p.4(4): 292-299.
10. Oishi N, Kanazaki S, Kataoka C, et al. *Acute-onset unilateral hearing psychogenic hearing loss in adults: Reports of six cases and diagnostic pitfalls.* ORL J Otorhinolaryngol Relat Spec. 2009;p.71(5):279-283.

Physical Examination of the Spine: 2nd edition



Authors: Todd J Albert, Alexander R. Vaccaro
Publisher: Thieme
Price: £48.63
Pages: 124

Reviewed by: Canisius Dzapasi, Spinal Specialist Physiotherapy Practitioner, Walton Centre NHS Foundation Trust, Liverpool.

Physical examination of the Spine by Albert and Vaccaro, in its second edition is an outstanding work that should be useful to any professional involved in the management of spinal conditions. I think the book is likely to be especially for those professionals who have not undergone formal training as spinal surgeons, as a quick reference. Such colleagues might include specialist physiotherapists and nurse practitioners, as well as medics with musculoskeletal/neurological interest. It might also be used to prepare for exams, for medical students or others.

Published by Thieme, it is a compact book (only 124 pages), presented concisely and in an easy-to-follow style. Its logical sequence makes the content easy to understand and remember.

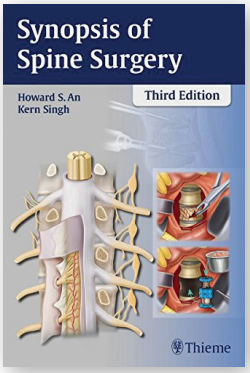
In terms of content, the first chapter (The Fundamentals) provides the basics of spinal examination - anatomy and function. The images are of high quality and provide a lot of information at a glance, and are laid out so as to be useful for quick revision. Sensory and motor testing follows immediately after descriptions of the functional pathways, providing a good perspective. Examination is explained in detail, step by step.

The cervical spine section gives detail on palpation with clear visual aides. This was especially useful from the Physiotherapy standpoint. Conversely, the investigations important in assessing the cervical spine are also presented effectively, backed up with clear images.

The thoracic spine and lumbar spine physical examination chapters provide more detail than might be expected in a book of this size. The examination techniques are explained with pictures, which represent a good guide for positioning and handling.

At $48.63, the book is expensive for its size, though the high price is justified on the basis of its high quality content.

Synopsis of Spine Surgery: 3rd Edition



Authors: Howard S An, Kern Singh
Published by: Thieme
Price: £71.99
ISBN: 1626230307
Pages: 316

Reviewed by: Ms Maggie K. Lee, Clinical Fellow in Neurosurgery, Walton Centre NHS Foundation Trust, Liverpool.

This is the 3rd edition by An and Singh. As per previous editions, it is well structured and concise. It contains information alike for novices in Spinal Surgery and for experts.

The aim of this book is exactly 'what it says on the tin', to offer the reader a comprehensive review of spinal diseases and conditions. Its layout is logical and leads the reader on a journey through the management of spinal pathology, beginning with anatomy, basic principles, physical examination, investigations, non-surgical management and surgery. All this, with many illustrations, radiological images and useful tables included.

It is packed with facts, without much narrative, which makes it a valuable resource of reference. The suggested reading list at the end of each chapter is a useful addition, although some of the references are not very up to date.

On the down side, the quality of reproduction of MRI images and clinical photographs is quite poor. And, although there is a legend for each image, more comprehensive labelling of these images would have been beneficial. And there are some labelling errors, in Chapter 10 (where the cervical spine level is mis-labelled) and in Chapter 14.

Overall, this book is one of the best in its class, and a 'must have' for students and trainees embarking on serious exploration of Spinal Surgery.

Personal Perspective: Spinal Stroke

Rosie Tween

1st May 2013 started like any normal working day apart from one thing – I felt a sudden pain in my mid to lower back as I was getting dressed. It was sharp enough to take my breath away but barely lasted a couple of minutes and was quickly forgotten. It was a glorious spring morning as I set off cycling to work but I was barely half a mile from home when I felt my bike pedals weren't moving around properly. I braked ready to get off and see what the problem was but when my feet touched the ground my weight just gave way beneath me and I collapsed in the road. I phoned my husband, David, who, with the help of a passerby, lifted me onto the back seat of the car and drove me to hospital. In the space of just over an hour I had lost power and sensation in both legs and my pelvis to just above my waist. I had been doubly incontinent having lost control of both my bladder and bowel. Was the creeping paralysis going to stop? Would it prevent me from breathing? I remember telling David that I loved him: I was terrified.

The staff in A&E were brilliant. In fact I couldn't fault the medical attention and investigation from start to finish. Living so near to Cambridge University Hospitals meant that I had rapid access to an extensive team of neurologists, many involved in different areas of research within the University. The initial diagnosis was a collapsed central disc and I knew that this was a clinical emergency likely to require urgent surgery to prevent permanent damage to the spinal cord. But no such luck! The MRI drew a blank, as did another one of higher up the spine. The diagnosis was not looking so good.

I was sent up to a ward where a urinary catheter was inserted and I was seen by the on-call Consultant Neurologist. He thought it most likely that I had suffered a spinal stroke causing a spinal cord infarction at thoracic level 10. Then, he told me that it was unlikely I would ever walk again. There isn't really any way of delivering such devastating news that won't cause distress. David was with me, and hearing it together helped; at least we could cry together. This provisional diagnosis had been reached as a result of taking a thorough medical history and carrying out a full physical examination. The MRI scan was also a key test; the absence of anything causing pressure on the spinal cord had been noted but I would need another scan a few days after the infarction or bleed to confirm that the blood supply had been disrupted. Spinal strokes are a rare condition, much less common than cerebral strokes: they account for about 1.2% of all strokes.

There were two other diagnostic possibilities: damage to the spinal cord through either an autoimmune response called Neuromyelitis Optica (NMO) or as a result of severe infection, bacterial or viral. My medical team began initial treatment modalities for both these possibilities. I started a short course of high dose steroids, a course of high dose intravenous antibiotics and high dose anti-viral treatment. A central line was inserted for five days of plasma exchange. I was seen by someone from the infectious diseases team who checked my recent travel history, any unusual contacts and requested various blood tests, which were sent to laboratories around the country. The specialist nurse did a lumbar puncture so that the CSF could be sent for full analysis, including an infection screen. I started to clutch at straws; as a regular rower and river swimmer, maybe I'd picked up some rare bug from the river water? An infective cause surely gave me the best prognosis. But I was well, had no fever and I think everyone knew it was unlikely. I'd had nursing experience of caring for someone with worst case NMO also known as Devic's disease. It is characterised by relapse and remission, severely deteriorating vision and paralysis that can require long term management with immunosuppressant therapy. Less than five days after suffering the shock of a diagnosis where I was to be almost certain of permanent paralysis, I now found myself favouring that over an NMO prognosis which could be both severely debilitating and forever uncertain. Not being able to walk again at least gave me some certainty and a point from which to start planning for the future.

I was determined to be strong. From day one I reflected on how lucky I was – I'd already lived 56 years of a full and interesting life, my body above my waist was ok: I was still me. The unit psychologist worked closely with me helping me to acknowledge loss and to start to process my grief. But it was a long time before I could start to work through my overwhelming feelings of guilt. Spinal cord injury (SCI) is a life changing event and impacts on the whole family, as well as the injured person. As a wife, mother to three children, daughter, colleague and friend to many – how could I not feel guilt?

Persistent neuropathic pain occurs in 40% of people who have suffered SCI. In my case the severe pain is characterised by burning and tingling in my pelvis, perineum, legs and feet alongside tightness to the point of thinking the skin is about to tear. The pain has been severely debilitating, and has had more of a detrimental effect on my quality of life than the paralysis itself. Specialist pain units with access to both clinical and psychological services are not readily or uniformly available. Clinical Pain management is driven by drug therapy, although the possibility of more invasive approaches, such as spinal cord or deep brain stimulation, were discussed. These were unlikely to be effective and were not easily available anyway.

Psychological based pain management provides rehabilitative treatment, often in a group setting, and can help develop different coping strategies, such as learning to pace yourself whilst still living an active life. Being forced to alter my pace of life, which included retirement on the grounds of ill health, caused me huge emotional distress. Eventually I was referred to the local mental health service and

received a course of Acceptance Commitment Therapy (ACT) over several months. This cognitive therapeutical approach, supplemented with courses in mindful meditation, proved a significant turning point in my approach to pain management. Acceptance has been the key to ownership and has reduced my dependency on the medical team, ultimately making me stronger and more able to define and use my own management strategies.

Rehabilitation plays a major role following SCI and I was fortunate to be referred to Stoke Mandeville Spinal Injuries Unit. My early experiences were bewildering, mainly because I suddenly realised that there were so many people who were there to learn how to walk again. Partly as a result of early diagnosis and intervention, complete SCI is now much less common than incomplete injury, which offers the possibility of at least partial recovery. My rehabilitation consisted of learning how to adapt to a different functioning body and to live independently from a wheelchair. It felt as though I'd been put in the remedial class - the group left to face the worst prognosis. Despite these overwhelming feelings of imminent failure, I did engage in an excellent rehab programme at Stoke Mandeville and eventually became fearful of being discharged home.

The real challenges began at home. Adapting to a real life environment, as opposed to the smooth hospital corridors with automatic doors, ramps to raised entrances and an accessible toilet on every floor, brought a new level of planning into every aspect of day-to-day life. Gone were the days of easy spontaneity. Each new tiny achievement was celebrated but there were many days when the exhaustion of just getting up, showered and dressed left me questioning what was the point of it all. The pain posed the greatest challenge and weakened me psychologically. Depression in chronic pain sufferers is well documented and the suicide rate among people with chronic pain is approximately double that for people who are pain-free. But I challenged those who questioned that I might be depressed; surely I was entitled to feel sad?

Recently I visited a local Primary School to lead an assembly. One child asked me how I managed to get dressed, puzzled as to how someone who can't stand can put on a pair of trousers. This question prompted me to tell the children that I can do almost everything I used to do before becoming wheelchair dependent, but that I sometimes need to do it a bit differently. Acceptance, a willingness to adapt and a good sense of humour have been key in enabling me to live a fulfilling and happy life again.

The charity Back Up[1] helped me to realise that life after spinal cord injury was still full of pleasure and potential, and I now volunteer for them, both as a mentor and a wheelchair skills trainer. On 1st July this year I climbed Mount Snowdon in my wheelchair, pushing myself up alongside a team of 16 women who helped to push and pull me to the top and down again.[2] We were the first all-female team to enter this challenge and raised over £20,000 for the charity. This was the highest amount ever raised by a single team and will help others who have suffered SCI to reach independence and fulfillment, as I have.

REFERENCES

1. The Back Up Trust - backuptrust.org.uk
2. Justgiving/fundraising/rosietween-womenofaltitude

How to prepare for the MRCP Neurology exam

Ann Donnelly
is a Neurology Registrar at the National Hospital for Neurology and Neurosurgery and Co-Editor of ACNR. She completed undergraduate training at University of Glasgow Medical School, with Neurology postgraduate training at Kings College Hospital, National Hospital for Neurology and Neurosurgery, and Guys and St Thomas'. She has also worked in medical publishing, first at the BMJ, where she imagined and developed the early model of what is now Doc2Doc and later at BioMed Central where she launched Alzheimer's Research & Therapy, Molecular Autism, and Stem Cell Research & Therapy. She is interested in Neurorehabilitation with a focus on patients with multiple sclerosis.

These are neurologists crossing the border,
Learning the genes and the prevalence order,
Causes of twitch, of vision poor,
The heredo-degenerative, and the rule of four,

(Apologies to WH Auden)

This is a personal view about how to approach this thrilling exam, which is your final gateway to the world of a Consultant Neurologist. This is a view based on experience and the gems passed on to me from many colleagues who have been successful throughout the years with some tips and information provided by Professor Shorvon on 'Cramming for the Exit Exam' Pre-course workshop of Neurology run by UCL Institute of Neurology. When my child asked me what thrilling meant, I explained "Exciting, but a little bit scary".

The best time to do the exam
This is a decision which only you may take. Statistically you are giving yourself a better chance when you leave it a little later in your training. It can work either way. Passed early, you've covered the curriculum and can spend the next four years consolidating and refining that knowledge, and keeping up with the demands of your e-portfolio. Later in your training, it provides an opportunity to tie up all the loose ends, to polish off your knowledge and get into the Consultant mind-set. Only you can know which is better for you.

When to start studying
Now.
Think tortoise not hare. This is an abstract type of exam, and will not only require you to recognise most neurological syndromes, and their differentials (see the mimics and chameleons articles in Practical Neurology, and the Bare Essentials). You will also need to be able to apply that knowledge practically and in a way that is relevant to your clinical practice as a Consultant. So know more than first line management, for common diseases, and the complications of the different treatments.

I would recommend that you take notes in every clinic, with every interaction, every CPC or Grand Round. Even one learning point per session will be priceless further down the line. Take notes as if you are doing it for someone else to read later (you are, future you!). With this in mind, that helps you to make more focused notes. I was a late adopter of the smartphone/iPAD resource of making notes (hence piles of beautiful yet half filled notebooks gathering dust on my bookshelf) but loved it. After every on call interaction.

The little nuggets gleaned (and in later years saved on my iphone) helped to hook the 'dry' text into my brain with every bit of learning. Ideally combine this with eportfolio reflections.

Early.

Baseline knowledge
Get out the curriculum and have a look. It is helpful to do some questions at the beginning. That will give you a clue as to where your main knowledge gaps are. Spot the nooks and the crannies that are dusty for you, and carve out more time than you might expect to review these – not all the subjects are weighted equally (see the table below for weighting of subjects).

We all work long days and many of us have family commitments, undisturbed hours in the library we may once have enjoyed are but a distant medical school memory. Reading on the 'Tube' (squished, standing), or listening to podcasts (the AAN/neurology or Lancet Neurology) and at work, when time allows, is needed. Late at night when you'd like a nap, 20 minutes can be squeezed in. Help is at hand in the form of revision courses (list below), online modules (Ebrainjnc), twitter tips (@abntrainees) and attending all the local teaching sessions your job will permit. I found YouTube an invaluable resource, for example EEG education https://www.youtube.com/user/EEGeducation.

My best friends throughout this were Practical Neurology and ACNR. If I ever felt saturated, desaturated or overwhelmed with the enormity of this beautiful intricate magical specialty, then a light hearted debate on clinical signs, or an unusual case was enough to draw me in again, to absorb me. These should be your companions to learning. They are up to date, and written by people who 'practise what they preach'. There are nuggets and insights and clear guidance.

Because the authors are people who love their subject, and use their knowledge from a practical point of view, they will hold your hand throughout this process of learning how to manage neurological disease. There are many interesting case reports, and thoughts about neurology. Every year a quirky little diagnosis will slink its way into the exam (Ciguatera, anyone?), and I can only imagine the smiles or sinking heart depending on whether you remember how an article ended.

Other essential foundations to your knowledge include guidelines from NICE, SIGN, and, of course, the ABN. This is a UK exam, and you need to know these by heart (or well at least). The diagnostic criteria for most neurological illnesses (GBS/CIDP/MND/MS/dementia/Parkinson's/headache syndromes) should be a good starting point, then in the course of your clinical work, you can observe how the specialists apply these, and 'square the circle' for patients who do not meet exact criteria.

Membership of the ABN is assumed, but also joining the AAN (at trainee level) is relatively inexpensive and allows access to their bank of questions and their comprehensive Continuum textbooks, which are brilliant at any stage of training. They also have a great collection of questions which you can do online. Ebrain is another excellent

source of learning material and the questions provided are from previous exams (see the Royal College of Physicians website too).

Imagine you are the on call Consultant now. As a Registrar you formulate a diagnosis and know first line treatments, but as Consultant you will need to know how to refine that diagnosis, and interpret investigations (imaging, neuroophysiology, visual field testing) usefully. Lists are essential (causes of ataxia and neuropathy, movement disorders in young people, progressive myoclonic epilepsies). An overview of the range of short term and long term treatment options, dose adjustments, complications of treatment, when to switch or stop. When you view your study from this perspective, then you will get the true value of it. This is not 'just another hoop'. This is your chance to clear the decks (make this your number one priority), to devote yourself to progressing and finessing your knowledge so you are ready for the next stage. To get the most return for your study, think clinically.

For me, reading was not enough, there was annotation, drawing, recording lists onto my phone for commuting. I found memory cards really helpful. Teaching others what you have learned always demonstrates your confidence with the topic. Study groups can boost morale and be a motivating factor if you can find the time.

I loved our local Grand Rounds. Nothing brings the list of something like progressive myoclonic epilepsies into clear focus like the knowledge that you may have a microphone in your hand one day, and a friendly Professor asking you to remind the room of that list. It's unfashionable to say it, but a little edge of fear helps me to remember things more clearly than anything else.

The arrival

Ultimately when the hour draws near, it is good to come back to the questions. The subjects are not equally weighted. The exam itself takes place in several centres where people may simultaneously be taking their theory of driving test. Apparently it can be ambiguous about when the exam begins, the clock starts ticking.

The examiners

Relax. Examiners want you to pass (if you've done the work). The questions can be complicated and seem obtuse. Sometimes it helps to take a step back. If it looks like X and it sounds like X, but there's one little anomalous detail. Then, is it X? This is your time to be a clinician. Is the anomaly a little clue to the diagnosis, or red herring? I cannot tell you, but looking back, I am sure that some anomalies are there to make you question your certainty (which is what real life medicine is like) but make a decision based on your "gut instinct". Sometimes they are there to prompt you towards another diagnosis. The skill in this exam is being able to differentiate between the two.

The point is, you need to go into this exam with a calm disposition. Breathe, read carefully, see the clues. Do not go down the rabbit hole – if this is a soft sign of another diagnosis (positive ANA), but all the clues are pointing to a much more likely diagnosis (clinical and radiological picture of NMO), then it's probably the one you think it is.

The examiners are people who love their specialty and expect you to know how to identify and manage their patients so they will give you clues and unlock the door to the right answer. Marks can be lost by overthinking.

Think about this exam, not as a barrier to your career ahead, but as your chance to finally bury yourself deep in your subject, and hopefully to emerge from the chrysalis of revision notes as a nascent Consultant Neurologist, maybe even getting a chance to write a few questions of your own one day.

I hope this is helpful, and I wish everyone the best of luck!

Professor Shorvon facts:

- Exam consists of MCQ - best of 5 (all plausible)
- 200 questions in 2 papers
- No negative marking – so guess if not known!
- Not like ABN self assessment – avoids ambiguity
- Also 'extras' (eg ethics)
- Mainly case scenarios – can be 'unworldly' in the sense of not common situations
- Will include data interpretation (neurophysiology, neuroradiology) and therapeutics
- Pass mark not fixed (currently) typically around 56% (113/200)

Exam knowledge and UK specific guidlelines	Royal College of Physicians https://www.mrcpuk.org/mrcpuk-examinations/advice-guidance-and-preparation UK guidelines: https://www.nice.org.uk/guidance/published?type=cg http://sign.ac.uk/ Curriculuum: https://www.jrcptb.org.uk/documents/2010-neurology-amendment-2013 Question weighting: https://www.mrcpuk.org/sites/default/files/documents/Neurology%20Blueprint%202015.pdf
Question banks	• Royal College of Physicians https://www.mrcpuk.org/mrcpuk-examinations/specialty-certificate-examinations/specialties/neurology • Sample questions https://www.mrcpuk.org/sites/default/files/documents/Neurology%20Blueprint%202015.pdf • Ebrain http://www.ebrain.net/ • AAN: https://www.aan.com/ • Comprehensive Review in Clinical Neurology: A Multiple Choice Question Book for the Wards and Boards: 1 Jul 2011
Baseline text	• Neurology: A Queen Square Textbook, Second Edition (Author: Charles Clarke and Robin Howard) • Clinical Neurology, 4th Edition Paperback – 30 Dec 2011 • Practical Neurology (especially the bare essentials and the 'mimics and chameleons')
Courses	• Leading edge neurology for the practising clinician: http://www.ucl.ac.uk/ion/education/courses/other/neurology/ • Birmingham movement disorders course • Cambridge Dementia Course http://www.cambridgedementiacourse.com/ • ILAE Oxford Epilepsy http://www.ilae.org/ • Edinburgh Neurology course • Keele Neuroinflammation course • Keele Headache course • Liverpool neuroid course: https://www.liverpool.ac.uk/neuroidcourse/

The Tom Isaacs Award

In memory of Tom Isaacs, who died in May 2017, The Van Andel Research Institute and The Cure Parkinson's Trust will introduce a new award to be presented at the annual Grand Challenges in Parkinson's and Rallying to the Challenge meeting on 27th & 28th September in Grand Rapids, Michigan, US.

The award is presented jointly by the Van Andel Research Institute and The Cure Parkinson's Trust in recognition of Tom Isaacs' vision that a cure for Parkinson's will be found, but greater value is gained from working with people with Parkinson's in this quest.

"During my time working in the Parkinson's field, I have come to realise there is a patent lack of communication between scientists, clinicians and people living with Parkinson's. There is no doubt in my mind that if we all worked together as a team, that this would unlock the gates to a wealth of new thinking, new ideas and, most importantly pave the way to a spate of breakthrough treatments." Tom Isaacs, the late President and Co-founder of The Cure Parkinson's Trust.

Tom died on 31st May 2017 aged 49 having lived with Parkinson's for 23 years – he pioneered for a cure for 18 years.

Launch of the 2017 QuDoS in MS programme

The 2017 QuDoS in MS Programme, established to recognise Quality in the Delivery of Services in Multiple Sclerosis, is now open for entry to teams and individuals working within the field of multiple sclerosis (MS). Now in its third year, QuDoS in MS highlights innovation and excellence in MS management and service delivery as well as the valuable contribution of those dedicated to improving the quality of life and experience of care for those with MS.

pharmaphorum media is delighted to once again be working in partnership with the Multiple Sclerosis Trust on this programme. It comprises both a recognition event and subsequent dissemination opportunities, and has the support and active participation of key industry stakeholders, including Biogen and Roche.

Entries are invited from MS specialist nurses, other nurses working in MS, allied health professionals including physiotherapists and occupational therapists, specialist registrars and consultants, pharmacists, GPs, and other healthcare professionals working in primary care, hospitals or the broader community.

The entry deadline is 5pm on Monday September 11th, 2017 with judging taking place early October.
Visit www.qudos-ms.com for further information.

WFNR Franz Gerstenbrand Award – Now open for entries

The World Federation for Neurorehabilitation (WFNR) Franz Gerstenbrand Award, now in its 5th year, is open for entries from clinicians, researchers and allied health professionals. The Award, worth £3000, recognises and rewards a neurorehabilitation project that has benefitted patients.

Professor Leonard Li, WFNR President said: "The WFNR announces its annual Award to coincide with Brain Awareness Week and to focus on the importance of neurorehabilitation for our patients".

Entries for the WFNR Award can come from any aspect of neurorehabilitation, for example a patient or clinic management initiative, research project, best practice development or the use of a new technological development. The Award encourages all professionals working in the field to enter, and special consideration is given to applications from those under 30 years of age.

Named after Professor Franz Gerstenbrand, in recognition of his continuous contributions to neurorehabilitation, the Award is open to WFNR members and non-members worldwide. The annual, single prize will be awarded as either a travel bursary to a clinical conference, professional development course or research project.

The deadline for entries is 30 November 2017, for more information visit: http://wfnr.co.uk/education-and-research/wfnr-award/

UKABIF Awards/ Film Competition

UKABIF has several Awards open in the run up to its 9th Annual Conference 'Navigating the future for brain injury survivors: health, rehabilitation and beyond', which takes place on Monday 13th November 2017 at the Royal Society of Medicine, 1 Wimpole St, London W1G 0AE.

The UKABIF Short Film Award, sponsored by Elysium Neurological, acknowledges, recognises and rewards a film that can inspire and educate all audiences about the impact of Acquired Brain Injury (ABI). Entries should be a maximum of five minutes long and should be an innovative, informative and a 'must-see' film that best narrates the impact of ABI. The Award is open to UKABIF members and non-members from the rehabilitation multidisciplinary team, doctors in primary and secondary care, case managers, personal injury lawyers, social care workers, voluntary organisations and care providers, to individuals with a brain injury, their families or carers.

The deadline for the Award is 30th September 2017 (see www.ukabif.org.uk/filmaward). The winner will received a £750 prize and two runners up will received £250.

There are three other Awards; the UKABIF Inspiration Award, UKABIF Clinician of the Year Award and UKABIF Lawyer of the Year Award. All three Awards are now open for nominations to recognise either the individual who inspires others in ABI, the clinician who goes the extra mile for their patients, or the lawyer that works tirelessly to obtain financial compensation for life-long support.

The deadline for Clinician of the Year Award and UKABIF Lawyer of the Year Award is the 31st October 2017. Further information see www.ukabif.org.uk
All the Awards will be presented at the UKABIF conference.

Miratul Muqit has recently received two awards recognising the contributions his laboratory has made to decipher the molecular mechanisms underpinning Parkinson's disease. Firstly, he has been awarded the 2018 Francis Crick Medal and Lecture by the Royal Society. He has also been awarded the 2018 Graham Bull Prize and Goulstonian Lecture by the Royal College of Physicians. He follows fellow Neurologists Martin Turner, Geraint Rees, Masud Husain and Mike Hanna who have been recipients of this award in recent years.

Getting it right first time for Neurology

A new national programme has been developed to undertake reviews in the NHS, one of which is neurology. The programme is called Getting It Right First Time (GIRFT 2017) http://gettingitrightfirsttime.co.uk/

The GIRFT programme is to be led by leading clinicians from across the NHS who will undertake reviews into a range of 14 medical and surgical specialities (Box 1). The clinical leads for the neurology GIRFT are Dr Geraint Fuller, Consultant Neurologist at Gloucestershire Hospitals NHS Foundation Trust and Professor Adrian Williams, Professor of Neurology, University Hospitals Birmingham NHS Foundation Trust.

Over the coming months Dr Fuller and Prof Williams will visit units to explore current practice and then provide a national report to make recommendations for neurology services to 'Get it right first time'.

The review details are not yet explicit although the Neurological Alliance and Sue Ryder state patient pathways and the need to address delayed transfers in care are two areas under consideration (NA 2017). We can also gain some insight into what reviews might contain by looking at possibilities by what the first GIRFT review (into general surgery) has uncovered. http://gettingitrightfirsttime.co.uk/national-general-surgery-report-published-2/

This review grouped findings into five themes including performance, choice, commissioning and care pathways as well as data and performance measurement (Abercrombie 2017).

Neurology services per se have been lacking adequate focus for some time despite the considerable work done by many at a policy level. The 2011 National Audit Office review of neurology services https://www.nao.org.uk/wp-content/uploads/2011/12/10121586.pdf highlighted the lack of an adequate focus on neurology services and the significant rise in hospital admissions. The trend in hospital admissions in neurology has continued with the NHS spending over £4.2 billion on neurology services in 2013/14 including funding for over 827 emergency admissions (NA 2017).

The Public Accounts Committee (PAC 2012) in its review of neurology services concluded that "services remain well below quality requirements…coordination of care for individuals is poor and there is a lack of integration between health and social services…". In 2015 the National Audit Office wrote a follow up report (PAC 2016) which said that the Government failed to respond to several of the PAC recommendations.

Hopefully GIRFT might produce significant changes to services – read ACNR for future updates from the Neurology Academy Ltd. www.neurologyacademy.org

GIRFT service priorities Box 1

1. Breast surgery
2. Acute and General Medicine
3. Cardiology
4. Respiratory
5. Geriatrics
6. Dermatology
7. Neurology
8. Gastroenterology
9. Diabetes and endocrinology
10. Renal medicine
11. Anaesthesia and Peri-operative medicine
12. Hospital dentistry
13. Intensive and critical care
14. Imaging and radiology

References

Abercrombie J (2017) General Surgery GIRFT National Specialty Report Royal College of Surgeons, Royal National Orthopaedic Hospital, NHS Improvement http://gettingitrightfirsttime.co.uk/wp-content/uploads/2017/07/GIRFT-GeneralSurgeryReport-Aug17v1.pdf

Timmins N (2017) Tackling variations in clinical care. Assessing the Getting it right first time (GIRFT) programme Kings Fund London

GIRFT programme website http://gettingitrightfirsttime.co.uk/news-blog/

Neurological Alliance and Sue Ryder (2017) Going the distance 2 Neurological Alliance

National Audit Office (2011) Services for people with neurological conditions NA London

National Audit office (2015) Services for people with neurological conditions progress review NA London

Public Accounts Committee Seventy Second Report (2012) Services for people with neurological conditions HM Government

https://publications.parliament.uk/pa/cm201012/cmselect/cmpubacc/1759/175902.htm

Public Accounts Committee (2016) Services to people with neurological conditions: progress review Twenty -fourth report of session 2015-2016 HM Government

https://publications.parliament.uk/pa/cm201516/cmselect/cmpubacc/502/50202.htm

Department of Health (2005) National Service Framework for Neurological Conditions DH London

NICE launches new evidence tool for medtech product developers

NICE's Scientific Advice service has launched an online tool to help developers of medical devices and diagnostics understand and generate the evidence needed to show their products are clinically and cost effective. This will help companies prepare for a dialogue with health technology assessment organisations and payers and potentially speed up time to market.

The Medtech Early Technical Assessment (META) tool has been developed in partnership with Greater Manchester Academic Health Science Network. The tool helps companies identify what evidence they have and what gaps need to be filled to satisfy payer requirements. It is a paid for service aimed at, but not limited to, small and medium sized companies.

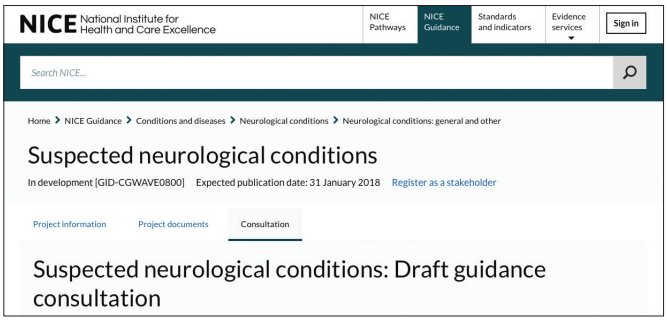
Leeza Osipenko, head of NICE Scientific Advice said: "Medical devices and diagnostics is a fast growing and highly competitive field. Healthcare systems are facing financial pressures and are keen to adopt transformative and cost saving technologies.

"We want to help healthcare systems get access to more products that meet such criteria and help companies develop these technologies and relevant evidence to demonstrate their value to patients and payers.

The META tool can be licensed for use by partner organisations working with medtech companies.

The tool was launched on 3 July by NICE chief executive Sir Andrew Dillon. See the NICE website at https://medicinesevents.nice.org.uk/meta

NICE draft guideline consultation – suspected neurological conditions



The draft guideline for suspected neurological conditions and its supporting evidence are out for consultation until 5pm on 19 September 2017.

You can submit comments on the draft guideline; this is a valuable opportunity to ensure that the guideline considers issues important to your organisation. The consultation page has all the information and documents needed to comment.

https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0800/consultation/html-content-2

For information/queries E. NeurologicalProblems@nice.org.uk

To list your event in this diary email Rachael@acnr.co.uk by 6th November, 2017

SEPTEMBER

FND 2017-The 3rd International Conference on Functional (Psychogenic) Neurological Disorders
September 6-8, 2017; Edinburgh, Scotland
www.fnd2017.org

Community Brain Injury – Developing a treatment plan for cognitive, communication and emotional changes
22 September, 2017; Ely, Cambridge, UK
Rachel Everett, E. courses@ozc.nhs.uk T. 01353 652165.

Brain Injury Rehabilitation Trust Conference
September 27-28, 2017, Glasgow, UK
www.birt.co.uk/conference

OCTOBER

JAMES PARKINSON – THE LONDON LEGACY – Parkinson's Disease Specialist Meeting
2 October, 2017; Medical Society of London
E. rcapildeo@uk-consultants.co.uk

ILAE British Chapter Annual Scientific Meeting
4–6 October, 2017; Leeds, UK
www.ilaebritishconference.org.uk
E. members@ilaebritish.org.uk

10th Practical Cognition Course
October 12-13, 2017; Liverpool, UK
E. sam.pickup@lmi.org.uk, T. 0151 709 9125 ex 103).
www.lmi.org.uk/pcc

ABN Autumn Meeting
12 October, 2017; London, UK
www.theabn.org/events

Recovery after Brain Injury: State of the Art 2017
13 October, RSM London, UK
http://ow.ly/ggIH30e2Cpi, E. tom@arni.uk.com

Making the Most – Non-Oral Therapies in Parkinson's
16 October, 2017; Southampton, UK
https://parkinsonsacademy.co/non-oral-therapy-roadshow/

Complex Epilepsy study day
17 October, 2017; Newcastle, UK
Jacqui on 07836 650782, E. jmassociates1@me.com

Making the Most – Non-Oral Therapies in Parkinson's
20 October, 2017; Manchester, UK
https://parkinsonsacademy.co/non-oral-therapy-roadshow/

NOVEMBER

Making the Most – Non-Oral Therapies in Parkinson's
6 November, 2017; Bristol, UK
https://parkinsonsacademy.co/non-oral-therapy-roadshow/

Brain Injury and Alcohol
10 November, 2017; Ely, Cambridge, UK
Rachel Everett, E. courses@ozc.nhs.uk T. 01353 652165.

Specialist Multiple Sclerosis Masterclass – MS Academy
22-24 November, 2017; Sheffield, UK
info@neurologyacademy.org, T. 0845 338 1726
Module 2: 15 June 2018

Palliative Care MasterClass
27 November, 2017; Manchester, UK
www.neurologyacademy.org

DECEMBER

Making the Most – Non-Oral Therapies in Parkinson's
4 December, 2017; Edinburgh, UK
https://parkinsonsacademy.co/non-oral-therapy-roadshow/

2018

FEBRUARY

Society for Research in Rehabilitation
Winter Meeting and 40th Anniversary
6 February 2018, The Watershed, Harbourside, Bristol BS1 5TX
E. patricia.dziunka@srr.org.uk, www.srr.org.uk

10th World Congress for NeuroRehabilitation – WCNR2018
7-10 February 2018 Mumbai, India
E: traceymole@wfnr.co.uk, www.wcnr2018.com

JULY

Movement: Brain, Body, Cognition
27-29 July, 2018, Harvard University, US – www.movementis.com

European Forum for Research in Rehabilitation Conference

Details: May 2017, Glasgow Caledonian University, Scotland.
Report by: Professor Pip Logan, University of Nottingham.
Conflict of interest statement: None declared.

The European Forum for Research in Rehabilitation held its 14th conference at Glasgow Caledonian University, UK, May 2017 hosted by Prof Frederike van Wijck as a joint meeting with the Society for Research in Rehabilitation, attracting over 274 multi-disciplinary delegates from 34 world-wide countries.

European conferences highlight the need for standard terminology to increase generalisability, applicability and rigour of research findings. The World Health Organisation International Classification of Functioning (WHO-ICF)[1] was reflected in many of the presentations and had been used to report how patients participate in activities giving the conference a constructive and inclusive atmosphere.

Workshops on implementing evidence based practice, research priority setting and managing chronic pain, provided an excellent learning environment for clinicians and researchers to share knowledge. These led seamlessly into presentations of the development of efficacious, feasible and acceptable rehabilitation interventions, such as soft robotic trousers for older people who fall. Most of the studies had employed the MRC Framework for Developing and Evaluating Complex Interventions[2] again providing a standard platform for global research.

The acute need to help patients stay in work, return to work and maintain work was highlighted by Dr Marnetoft from Sweden in his lecture on vocational rehabilitation. He warned that this is not an easy task, explaining that assistance is provided by a number of different organisations: insurance companies, employers, health services and local authorities. Whereas his research findings suggest that the best person to lead the vocational rehabilitation process is the supported patient.

Kate Allatt, a stroke survivor continued this theme by describing how after three hours of rehabilitation each day she was motivated to continue on her own. She challenged the audience to research patient's engagement with rehabilitation and preventing isolation. She finished her lecture by encouraging clinicians and researchers to communicate with patients via social media.

Stroke rehabilitation research was prominent across the conference with Professor Peter Langhorne (pictured) from Glasgow delivering the prestigious Peter Nichols lecture. His overview of the evidence base for stroke rehabilitation using the categories: can it work, does it work, is it worth it and can we implement it, sent a clear message that stroke rehabilitation is effective but complex. He suggested that systematic reviews to answer specific questions might be more fruitful than one larger multicentre trial. This concept was still in the delegate's minds when they heard about a trial of rehabilitation provided by carers, in 14 Indian locations (n 1250). The results were neutral but the trial demonstrated a growing demand for research into rehabilitation.

1. http://www.who.int/classifications/icf/en/
2. Craig BMJ 2008:337:a1655

End of Life in Disorders of Consciousness (DoC)

Conference details: March 24, 2017, London, UK. ***Report by:*** Dr Sarah Crawford, Consultant Clinical Neuropsychologist, RHN & The Rt.Revd. Dr Christopher Herbert, Visiting Professor of Christian Ethics, University of Surrey. ***Conflict of interest statement:*** None declared.

The conference on End of Life in Disorders of Consciousness (DoC) was held in London at the Royal Hospital for Neuro-disability (RHN) in Putney. RHN is a national medical charity providing both post-acute rehabilitation and continuing care for adults with complex neuro-disability. Providing services for patients in DoC, i.e. vegetative and minimally conscious states (VS and MCS), has been a specialism of the organisation for many years. Current services for these patients include both short-term post-acute assessment and disability management, and also longer-term care for patients in DoC who need highly specialist ongoing care. This conference aimed to bring together professionals and carers from a range of specialities to discuss clinical, ethical and legal issues relating to end of life decision-making and care for people in DoC.

The first speaker was Dr Amy Kingston, Consultant in Palliative Medicine, St George's Hospital and Trinity Hospice. Dr Kingston provided an overview of key documents and practice guidelines in managing end-of-life care and discussed the importance of integrating 'curative' and palliative care, since current evidence suggests that both quality and length of life are improved when there is good symptom management.

The keynote speaker for the day was Professor Derick Wade, Professor of Neurological Disability. Professor Wade gave an overview of the legal cases that have shaped the current UK situation with regard to end of life in DoC, particularly withdrawal of clinically assisted nutrition and hydration (CANH), and the current necessity to take all such decisions to the courts. He argued that the process of this evolution has led to an over-reliance on specific diagnostic labels (i.e. VS versus MCS) and a risk-averse culture in which clinicians can feel obliged to do everything possible to prolong life. He outlined key clinical, legal and economic evidence in this field and made a thought-provoking case for framing DoC as a continuum rather than two dichotomous diagnostic labels, and for decision-making to be done following the best-interest principles of the Mental Capacity Act (2005), with a suggested move away from routine court involvement.

Legal principles in this area were then discussed in further depth by Mr Yogi Amin, National Head of Public Law, Irwin Mitchell LLP, who provided useful insights into relevant case law developments in an area that continues to evolve.

Professor John Saunders then discussed the issues from an ethical perspective, considering the meanings of concepts such as consciousness, futility, rights and dignity in relation to this area.

The afternoon session opened with some personal reflections from Reverend Geoff Coyne, RHN Chaplain. Rev. Coyne talked about his perspective as a Christian Minister that all people who are living and breathing, regardless of their level of consciousness, have a spirit and therefore equal spiritual value. He shared his experiences of the wide variety of interpretations of life and death that he sees in the relatives of people in DoC in his pastoral care role at RHN.

This was followed by a talk from Mr Jim Beck, Healthcare & Welfare Lawyer at the Office of the Official Solicitor who talked about the role of his office in serious medical cases in the Court of Protection. Mr Beck explained that the diagnostic distinction between VS and MCS remains significant as, currently, treatment for people in permanent VS is deemed futile by virtue of diagnosis, whereas cases in MCS require a balance-sheet exercise. He also provided useful insights into some of the practical issues that can cause court decisions to be delayed, such as failures to conduct the right tests or to rule out other causes.

Further consideration of the ethical issues in this field was provided by Professor Raanan Gillon, Emeritus Professor of Medical Ethics, Imperial College London. He suggested that DoC is currently treated differently from other life and death contexts, such as decision-making in intensive care units, and gave the opinion that when best interests are agreed by all parties the case should not have to be heard by the Court of Protection.

This was followed by a talk from Ms Veronica English, Head of Medical Ethics, British Medical Association (BMA), who gave an overview of the role of the BMA in advising medical professionals, and the evolution of this guidance over time. She argued that clarity around the diagnostic and legal issues is essential for the BMA to be able to advise its members, and agreed with the view expressed by some of the other speakers that refining protocols is likely to remove the need for routine court approval of end of life decisions in DoC in the future.

The final speaker was Dr Andrew Hanrahan, Consultant in Rehabilitation Medicine and Neurological Disability, RHN, who provided a summary and final comment on the day. He described how the Royal Hospital for Neuro-disability had provided a platform where different and differing views had been expressed, listened to and challenged. He concluded that society and the professions needed to develop a new relationship with death and dying, seeing it as a social event rather than an arbitrary medical milestone on a temporally determined process.

Throughout the day there were opportunities for questions and discussions from the attendees, which enabled further insights and debates to be aired. Interesting discussions included questions about healthcare economics and the role of public finances in supporting people with DoC at the possible expense of financing care for those in other conditions, a suggested shift towards routinely asking whether it is right to continue with treatment rather than withdraw treatment for all patients in long-term DoC, and discussion around whether CANH is a 'right' or a 'treatment'.

This fascinating day highlighted the complex and often emotional issues in this area, and the endeavours of professionals from a range of clinical, legal and related backgrounds to have clarity, professionalism, and compassion in working with these patients and their families.

3rd European Stroke Organisation Conference – ESOC 2017

Conference Details: 16 to 18th May 2017, Prague, Czech Republic. ***Report by:*** Angelika Zarkali, Neurology Registrar. ***Conflict of interest statement:*** None declared.

Prague has a long tradition in science, literature and the arts, with the first university in central Europe, Universitat Karlova, founded in 1348. It is also one of the most visited cities in Europe. Thus, it seemed fitting that it held the 3rd annual conference of the European Stroke Organisation (ESO) in May 2017. Over three full days, 4200 delegates from 110 countries came together in Prague to debate, discuss and share knowledge on recent advances on every single aspect of stroke care, from prevention, to acute management, neuroimaging, rehabilitation, genetics – and the list goes on!


View from nearby Vysehrad

The conference programme was abundant and included two pre-conference meetings on Monday the 15th of May; the 3rd annual ESO-EAST workshop, where delegates from 23 Eastern European countries came together to improve stroke care in Eastern Europe and the ESO Trial Alliance Workshop, where more than 120 researchers across Europe discussed ways in which better European collaboration can be achieved in stroke research.

Over the next three days of the main conference, we were treated to a vast choice of high quality sessions. There were multiple parallel sessions, including for the first time four sessions specifically tailored for allied healthcare professionals, as well as workshops on various clinical stroke syndromes, acute management, neuroimaging, secondary prevention, and research methodology. Finally, with more than 1500 posters to view during breaks, the evening guided poster-walking sessions and an excellent exhibition, we were extremely busy for the whole duration of the conference!

Importantly, the conference provided an update on major clinical trials. During the opening plenary, after an introductory welcome to the conference and Prague we listened to results from many large clinical trials:

- The CLOSE and Gore-REDUCE trials, both showed that Patent foramen ovale (PFO) surgical closure, significantly reduces the risk of recurrences in young adults with cryptogenic stroke.
- Next, the DAWN study gave the extremely hopeful message that the treatment window for stroke has widened, with mechanical thrombectomy preventing disability in patients with severe strokes and "mismatch" on imaging, up to 24 hours from symptom onset. In addition, there was no significant difference in stroke related mortality or intracranial haemorrhage in the thrombectomy treated patients.
- The PICASSO study, showed that probucol can be used to reduce cholesterol level and risk of recurrent events in patients with ischaemic stroke who have high risk of cerebral haemorrhage.
- The NOR-TEST study showed that tenecteplase is as efficacious and safe as alteplase in acute stroke.

More detailed results from the opening plenary along with interviews of the primary investigators can be found here: https://goo.gl/UHlkFu

In the afternoon of the same day, the presidential symposium continued the update on major clinical trials after the presentation of well-deserved awards; the Presidential award to Professor Joanna Wardlaw from the University of Edinburgh, ESO Research Excellence Award to Daniel Strbian from the University of Helsinki, and three of the five Young Investigators awards to UK based researchers, Shane Lyons, Vafa Alakbarzade and Alan Cameron. Important findings from the presidential symposium were:

- The TO-ACT study, showed no benefit from endovascular treatment (thrombolysis or thrombectomy) versus anticoagulation in cerebral venous thrombosis.
- Similarly, the TALOS trial did not show positive results; although citalopram use was safe in ischaemic stroke, there was no change in functional outcome or recurrent events.
- The VISTA trial showed good functional outcomes of thrombectomy, with an odds ratio of improved disability of 1.94 favouring thrombectomy and no significant change in mortality. The efficacy of thrombectomy and functional outcomes were significantly related to time from onset of stroke to puncture, reaffirming the previous moto of "time is brain".
- The HERMES collaboration presented data that could help guide patient selection for thrombectomy, showing that the benefits of thrombectomy are greater in patients with smaller ischaemic core size on CT-perfusion and MRI while it remains effective for a volume up to at least 70mls.
- Finally, the TESPI trial advocated the use of thrombolysis in patients >80 years old within 3 hours of onset.

More details on the trials presented at the presidential symposium can be found here: https://goo.gl/sz5s6O

Finally, on the last day of the conference, we heard the results of important Late-Breaking clinical trials:

- The SPACE-2 trial added to the evidence of low periprocedural complications of carotid endarterectomy and stenting in patients with asymptomatic carotid artery disease.
- The PRASTRO-I study investigating prasugrel, a new platelet inhibitor, less reliant on resistance, showed no significant difference in stroke, myocardial infarction or other vascular disease between patients treated with prasugrel and those treated with clopidogrel. However this did not reach the predefined non-inferiority threshold.
- Finally, both the ANSTROKE and GOLIATH trials showed no difference in functional outcomes between patients who received endovascular treatment with general anaesthesia and those who received sedation.

Many more studies were presented throughout the whole of the conference over more than 50 parallel sessions and 2 guided poster-walks; too many to report. But with all abstracts published online at the European Stroke Journal, you can read to your hearts content! https://goo.gl/3ysrzE

In addition to updating us in scientific advances, a recurring theme throughout the whole of the conference, was that of international collaboration. The move towards a more organised, collective effort to improve stroke care and the emphasis on the global aspects of stroke became evident from the first day of the conference, when the ESO and the Stroke Alliance for Europe (SAFE), signed a Memorandum of Understanding pledging both organisations to work together towards improving stroke care in Europe.

Next, we saw the launch of the Burden of Stroke in Europe report (http://strokeeurope.eu/) which presents sobering data on the predicted increases in coming years; with a predicted number of 819,771 stroke events in 2035, a 34% increase from 2015 and estimated approximately 4,6 million people living with stroke in Europe at that time, both the economic cost to healthcare systems and the pressure to services will increase. The importance of improving stroke care delivery was strongly highlighted in the report that called for a national stroke strategy for each European country.

Finally, the joint ESO – WHO session on Global Perspectives of Stroke, explored themes such as the effects of poverty on prevalence and outcomes, regional variations in individual risk factors and the emergence of air pollution as a stroke risk factor.

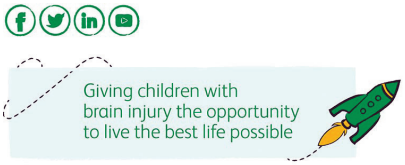
Overall, the 2017 ESOC was an amazing conference with a wealth of scientific presentations, practical workshops, ample networking opportunities and an emphasis on global perspectives and international collaboration; all in a beautiful, historic and most importantly sunny city.

I am definitely looking forward to the 4th European Stroke Organisation Conference, in May 2018, in Gothenburg and hopefully you are too!

National Paediatric Brain Injury conference 'Through the Looking Glass: Rehabilitation after Brain Injury in Children and Young People', The Children's Trust

Conference details: 15 June 2017, BMA House, Tavistock Square, London, UK. ***Report by:*** Dr Lorna Wales, Research Professional Lead, The Children's Trust, Occupational Therapist, BACD-Castang Fellow. ***Conflict of interest statement:*** None declared.

This year The Children's Trust held its first national paediatric brain injury conference at BMA House (British Medical Association) supported by Irwin Mitchell. This stunning venue, situated in the centre of London, made a particular impact on what was a beautiful summer's day. The delegates were able to enjoy the historic courtyard gardens and the speakers were delighted to present in the opulent Grand Hall.



The conference

The conference attracted over 200 delegates including medical, allied health, nursing and legal professionals, in addition to commissioners, community and commercial partners and associated organisations.

After the initial welcome and introductions from Maggie Clancy, Director of Clinical Services at The Children's Trust, the chair, Dr Andrew Curran, Consultant Paediatric Neurologist, Alder Hey Hospital, Liverpool, was introduced to the audience. His enthusiasm and passion for children and young people with brain injury encouraged active participation as he successfully steered the day.

The programme was headlined from a patient and parent perspective. The overall theme was rehabilitation and Ryan and his father Mark gave important insights into their experience of residential rehabilitation following Ryan's acquired brain injury (ABI). They presented a personal and, at times, a very honest account of their placement at The Children's Trust. Mark and Ryan stressed the value of family support from a variety of sources including tea around the table with other families, the nursing staff in addition to the formal support offered by the psychosocial and therapy teams. They were very engaging and it stimulated a prolonged question and answer time.

A description of the 24-hour multidisciplinary approach to rehabilitation was expertly presented by Maggie Clancy and Dr Carolyn Dunford, Head of Therapy and Research at The Children's Trust. This session highlighted the importance of a 24 hour collaborative goal-orientated approach to rehabilitation for children, young people and their families.

Invited speaker, Dr Richard Appleton, Consultant and Honorary Professor in Paediatric Neurology, Alder Hey Children's Hospital, Liverpool, reflected on the changes in delivery of rehabilitation following an ABI and the ongoing challenges which prompted some interesting discussions. He shared a best practice exemplar "Jack's Journey", from a 2004 Department of Health document which forms part of the National Service Framework for Children, Young People and Maternity Services. He reminded the audience of its on-going relevance.

This was followed by Dr Jenny Jim, Principal Clinical Psychologist, The Children's Trust who presented 'SPECS – seeing brain injury clearly', a two-day training package which has been developed for all staff working with children & families with ABI. This programme aims to enhance psychosocial care by increasing knowledge and confidence around this complex topic. Preliminary learner feedback has been extremely positive. A number of delegates enquired about commissioning it for their own services.

Lunch provided an excellent opportunity to network and visit exhibitors from a variety of service provider and commercial trade. At this time the delegates were also able to view the poster presentations and talk to the authors.

The afternoon session started with the challenging presentation of Dr Chris Kidson, Consultant Paediatric Intensivist, NHS Greater Glasgow and Clyde. This was a fascinating talk on the ethical dilemmas faced by healthcare professional when making quality of life decisions with children and young people in disorders of consciousness (DOC). He described how complex this topic was when associated with children and their families in comparison to an adult in the acute period after injury and what is in everyone's best interests. It was very thought provoking and the audience were left giving serious consideration to the content of his talk.

This was followed by a joint presentation by Dr Lorna Wales, Research Professional lead at The Children's Trust and Nancy McStravick, a parent partner on behalf of the Stroke Association and Royal College of Paediatrics Guideline Development Group. They shared their experiences of developing and disseminating the new Stroke in Childhood Guideline that was launched in May 2017. Nancy made the point that guidelines such as these are crucial and in this circumstance is a guideline that saved her daughter's life, reminding the audience of the importance of guideline development. The parent involvement in this project was extensive and the ensuing discussions by the delegates served to show the influence parents can have on all guideline development.

The final presentation was delivered by Dr Paramala Santosh, Consultant Child & Adolescent Psychiatrist, King's College London and visiting Consultant at The Children's Trust. The focus of his talk was on the personalised neuropsychiatric approach to paediatric ABI which remains a challenging topic.

Dalton Leong, Chief Executive, The Children's Trust closed this inaugural inspiring day with a summary of the topics reinforcing the importance of the role of rehabilitation for children, young people and their families following acquired brain injury.

Overall, the conference was in a great location on a fantastic summer's day, ending with a drinks reception in the stunning courtyard. The topics covered were interesting and inspiring and highlighted areas of future research and service development.

TNA UK Joint Patient & Healthcare Professionals Conference

Conference details: 3 June 2017. ***Report by:*** Dr Robert Coveney, Dental Surgeon. ***Conflict of interest statement:*** None declared.

The day was attended by a wide range of healthcare practitioners (HCPs) ranging from neurosurgeons, MS nurses, dentists to budding students, along with a large number of patients and carers.

Session 1: Diagnosis

Prof Zakrzewska invited four patients, with different diagnoses and histories, to speak about their prior or current symptoms. The four patients respectively had experienced; typical TN, atypical TN, SUNA and TN secondary to multiple sclerosis. The histories were put before a medical panel containing a neurosurgeon (Mr. Owen Sparrow), a neurologist (Prof. Turo Nurmikko) and a consultant of oral surgery (Prof. Tilly Loescher).

Following this interesting Q & A, Professor Zakrzewska continued her talk which highlighted the difficulty in reaching diagnosis (e.g. how cracked tooth syndrome and TN have a lot of overlap in their sensations). This leads to a difficulty in creating a simple questionnaire or a diagram that represents any one person's experience.

Session 2: What does brain imaging tell us about trigeminal neuralgia?

Professor Turo Nurmikko presented on MRI scans and their usefulness in diagnosing and predicting treatment outcomes for trigeminal neuralgia. The session highlighted how MRIs have led to a reduced need to just open and 'explore' the posterior fossa. MRIs rarely gave false negatives (no compression/contact of the nerve). With the advancement of the MRI technology, it is now possible to differentiate between:

- A contact between vessel and nerve.
- A compression between the vessel and nerve.
- A compression and pushing away of the nerve.

Rachel Coates & the University of Leeds

Dr Rachel Coates, a Psychologist, made an appeal for potential study on cognitive impairment whilst on and off of medication. She appealed to members to contact her by email, r.o.a.coats@leeds.ac.uk, if they so wished to participate.

Session 3: Additional support for patients – HCPs only

Two Clinical Nurse Specialists, Artemis Ghiai and Mandy Lodge talked about their roles in facilitating patients through all aspects of trigeminal neuralgia. Jillie Abbott from the Trigeminal Neuralgia Association UK explained about the essential support provided by TNA UK.

Session 4: Medications

This session focused on group activities. The membership jointly wrote down their first, second, third and – if applicable – their fourth prescribed medications. The effectiveness of each was discussed alongside why the medication was stopped (e.g. side effects or the drug stopped providing pain relief.

Meanwhile, the HCPs discussed what they believed the best first and second line therapies were for trigeminal neuralgia. The general consensus was carbamazepine should be the first line, as per NICE guidelines.

Professor Zakrzewska discussed the importance of establishing these guidelines, especially in the light of many patients not being prescribed carbamazepine as the first line.

Session 5: Outcome measures in TN & why they are important

An interactive session by Dr Richel Ni Riordain honed in on what TN patients feel are the best measures of 'success' from a medication. Some examples included:

- As few side effects as possible.
- Better function in a work environment & being able to carry out daily activities.
- Complete and long lasting remission from pain.
- No interactions with other drugs.
- Minimal or no loss of effectiveness with time
- General better social interactions.

These expert patient panels, reading through literature and further discussions will allow us to be able to develop a true outcomes criterion for trigeminal neuralgia. Hopefully, this will lead to a questionnaire to help best plan, effectively regulate and measure outcomes.

Session 6: Surgery for TN

Anne Eastman related her story of TN. Anne's tale, which spoke of her misdiagnosis and journey through fear into pain-free life, was hard hitting.

Mr Owen Sparrow, retired neurosurgeon, and his colleague, Imran Noorani, then discussed the surgical outcomes based on 30 years of data they have followed up. Mr Noorani highlighted that older patients tended to have less MVDs and more needle-based procedures. He highlighted that if pain reoccurs, usually it is at a much reduced level which means that medication is usually effective. Long term pain relief statistics are the same, no matter what vessel (be it vein or artery) is moved.

Finally, Professor Tilly Loescher spoke about stereotactic radiosurgery (sometimes called gamma knife). Originally designed for minimally invasive treatment of brain tumours, it has now evolved for use in other conditions, such as TN. Currently, TN is only commissioned (on the NHS) to be treated in two units – London & Sheffield. A high proportion of patients will get numbness following treatment and a 5% proportion will get 'painful numbness' or dysesthesia.

PREVIEW: Encephalitis Conference

Conference details: December 4th, 2017; London, UK.

Neurologists interested in learning about the latest developments in encephalitis are invited to attend the 2017 Encephalitis Conference in London on Monday, December 4.

The annual conference, organised by the Encephalitis Society, will once again feature a multi-disciplinary panel of international experts speaking on a wide range of topics related to encephalitis.

Audience members typically come from a variety of backgrounds, including scientists, researchers, clinicians, other healthcare professionals, solicitors and charity members.

It is also viewed as an ideal opportunity for individuals to network with experts involved in the study of the condition during a drinks reception at the end of the conference.

An application for CPD Points and APIL credits has also been submitted.

Places are free for professional members of the Encephalitis Society. Visit www.encephalitis.info/professional for further details and to book your place today.

Ask your patients if having children is part of their plan

UK/UKCPX/16/0031a
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