A Representative Collection of Previously Published Articles

2018 ANNUAL HIGHLIGHTS OF THE RESIDENT & FELLOW SECTION
NAVIGATING YOUR CAREER

Make this your stop for comprehensive information on professional development at every career stage, including medical student, resident, fellow, junior faculty, senior faculty, and advanced practice provider. Look for the latest advice and information through a variety of interactive formats: one-on-one consults, 30-minute mentoring sessions, small group talks, and panel discussions.

Attend the Faculty & Trainee Reception and Meet the Neurology Resident & Fellow Section Editors and Editorial team

Monday, April 23 • 6:00 p.m.–9:00 p.m.
J.W. Marriott, Diamond Ballroom

Experience a unique place for undergraduate and graduate attendees to network with peers, find information about residency programs, on pursuing fellowships and/or careers in neurology academics, research, or practice, and get recognized for their scholarships/awards.
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**About the Cover:** From the article: Clinical Reasoning: A 58-year-old man with progressive ptosis and walking difficulty by Pei-Hsin Kuo, MD, Raymond Y. Lo, MD, PhD, Kurenai Tanji, MD, PhD, and Sheng-Han Kuo, MD, Neurology July 4, 2017, 89 (1) e1-e5.

Histochemical analyses of the muscle biopsy

(A) Succinate dehydrogenase (SDH) stain (100x) shows muscle fibers with increased staining, indicating mitochondrial proliferation (arrows). (B) Combined SDH (blue) and cytochrome c oxidase (COX) (brown) stain (100x) show COX-negative fibers with strong SDH stain, demonstrating muscle fibers with respiratory chain defects with corresponding mitochondrial proliferation (arrows).
section editor

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John Millichap is a pediatric epileptologist in the Comprehensive Epilepsy Center, Ann & Robert H. Lurie Children’s Hospital of Chicago, and Assistant Professor of Neurology and Pediatrics at Northwestern University Feinberg School of Medicine. Millichap completed residency in pediatrics at the Brody School of Medicine, and held fellowships in Child Neurology and Clinical Neurophysiology / Pediatric Epilepsy at Children’s Memorial Hospital, Northwestern University. Millichap has over 35 peer-reviewed publications on pediatric neurology, epilepsy, and neuroinfectious disease. Current clinical practice utilizes a multidisciplinary team approach to the diagnosis and treatment of epilepsy and comorbidities. As a member of the academic faculty, he is involved in the education of trainees and grant-funded clinical research concerning epileptic encephalopathies. Millichap is an avid writer himself and enjoys encouraging resident and fellow contributions to the medical literature.

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Roy Strowd, Assistant Professor of Neurology and Oncology, is a neurologist and neuro-oncologist at the Wake Forest Baptist Medical Center. He graduated magna cum laude from Duke University in 2005 and from the Wake Forest School of Medicine in 2009. He completed residency in Neurology at Wake Forest Baptist Medical Center in 2013 where he served as Chief Resident. He pursued fellowship training at Johns Hopkins, completing the clinical and research Neuro-oncology Fellowship Program as well as dedicated training in medical education research through a fellowship supported by the American Academy of Neurology’s Medical Education Research Training Fellowship. Strowd has clinical research interests in drug development and response assessment in neuro-oncology as well as medical education interests in exploring optimal approaches for teaching health care professionals at multiple levels of training. Strowd is active in medical education, academic scholarship, and scientific research at both the local and national levels and truly enjoys each opportunity to mentor residents and fellows throughout neurology.

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Pouya Khankhanian is an adult neurology resident at the University of Pennsylvania in Philadelphia, and a researcher at the Center for Neuroengineering and Therapeutics. He graduated with a degree in applied mathematics from the University of California at Berkeley before getting his medical degree at the University of California, San Francisco. His research interests include bio-statistics, genetics and genomics, and multiple projects under the umbrella of “big data research,” with focuses in multiple sclerosis and epilepsy. His free time is spent either in the great outdoors, fostering pets, or home-brewing beers and wines.

Ariel Maia Lyons-Warren, MD, PhD

Ariel Lyons-Warren is a child neurology resident at Baylor College of Medicine in Houston Texas. She earned her Bachelor of Arts from Johns Hopkins University with a major in neuroscience and a minor in writing seminars. Prior to starting the medical scientist training program at Washington University in St. Louis she spent 6 months working in a London theatre, backpacked across Europe and then lived on a communal farm in Israel for 6 months. Her PhD research focused on the role of inhibition in temporal coding and she continues to be interested in how inhibition shapes neural circuits. Her clinical interests include medical education, palliative care, and sensory processing disorders.

Emer McGrath, MD, PhD, MRCP

Emer McGrath is an adult neurology resident at Massachusetts General Hospital and Brigham and Women’s Hospital Partners Neurology program. She completed her MD and PhD at the National University of Ireland, Galway. She trained in clinical epidemiology and biostatistics during her PhD, focusing on the epidemiology of stroke and atrial fibrillation. Her research focuses on the clinical epidemiology of stroke, vascular disease, and dementia. Her clinical interests include cognitive and vascular neurology.

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Steve O’Donnell attended the University of Rochester, where he studied political science and economics. Having no intention to go into medicine, he worked for four years in jobs that included fundraising for a presidential campaign, a non-profit public health organization, and as an Emergency Medical Technician. It was the latter experience that pushed him towards medical school and an unexpected return to the University of Rochester where he obtained his MD. He is currently at the University of Utah and will finish his residency in adult neurology in 2017 and then will pursue a fellowship in vascular neurology at the University of Washington.

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The Neurology Resident & Fellow Section

John J. Millichap, Roy Strowd, Kathleen Pieper

The history of the Neurology® Resident and Fellow Section (RFS) began in 2004 when the Resident & Fellow "Page" was launched with the mission to keep our readers up to date on issues related to training and career considerations as well as support the development of lifelong learning skills. The RFS was founded by Robert "Burch" Griggs, then the editor-in-chief of Neurology, and Karen Johnston, associate editor, who passed the reins to Mitch Elkind several years later. By then, the "Page" had grown to a "Section," with articles appearing weekly and a growing team of editorial members. Currently, the RFS is trainee-run by an editorial team of more than 20 neurology residents and fellows with the responsibility for reviewing, editing, and publishing articles. Residents are selected annually through a competitive process that attracts dozens of applicants and each will serve a three-year term. Past editorial team members have gone on to other important editorial activities, at Neurology and elsewhere, and they have found the experience a formative part of their careers. Dr. John Millichap, a former editorial team member and the current RFS Section Editor, assumed leadership of the section from Dr. Elkind in 2015. He is joined by Deputy Section Editor Roy Strowd, another former editorial team member. Photographs and brief biographies of the current Resident & Fellow Section editorial team can be found in this Highlights booklet.

The number of submissions to the RFS has steadily increased dramatically (from 12 in 2004 to 665 in 2017), and the quality of published manuscripts has improved. Over the years, the RFS has also introduced several subsections, which focus on (1) clinical neurologic education, such as Clinical Reasoning; Pearls & Oysters, Child Neurology, and Teaching NeuroImages; (2) graduate medical training, such as Journal Club, Global and Community Health, and Education Research; and (3) career issues, such as Emerging Subspecialties in Neurology. In addition, there are special subsections such as the Right Brain section which provides an outlet for creative writing, and Mystery Case section that engages readers in interactive discussion of critical aspects of clinical neurology. Descriptions of these subsections appear in this Highlights booklet and include one the top representative articles published in the past year as selected by the RFS editorial team members.

The RFS editorial team members have initiated and developed multiple unique projects including podcasts (beginning in 2007), weekly E-Pearls (2008), an annual Writing Award (first given in 2009), and our website (launched in 2010). Our ongoing Call for Authors program, in which trainees throughout the world have the opportunity to sign up to write articles on selected topics, was launched in 2012. In 2012, we also began making all Teaching NeuroImages available as teaching slides. In 2014, members of the RFS editorial team were awarded the American Academy of Neurology Education Research Grant to study the role of mentored peer review of journal articles as a way of teaching evidence-based medicine and peer review skills to residents. The research project involved residents at nine US residency programs, and the results were presented at the AAN and other national meetings. In 2015, Luca Bartolini, editorial team member of the RFS, developed his original idea for "Practice Current: An interactive exchange on controversial topics" in collaboration with the editors of Neurology® Clinical Practice (NCP). This has become a wildly popular section of NCP that aims to identify and discuss difficult clinical scenarios and diseases with conflicting or insufficient evidence regarding diagnosis or treatment. Other notable successful initiatives include the Clinical Reasoning book of previously published cases compiled to provide an educational resource for trainees and program directors, and the establishment of a RFS mentor-mentee pilot program designed to pair new RFS team members with recent graduates of the section. In years to come, we hope that this program may serve as a structured model for bringing new, young peer reviewers into the process, even outside the RFS itself.

This year brought many changes and to Neurology and the RFS. Most notably is the extensive design and formatting changes in the print Neurology and the updated website. The new RFS page has exciting new features such as RSS feed for the expanded blog, new e-Pearls formatting, listings of the latest RFS articles, and online survey platform for the Mystery Cases. Following feedback from our readers, we included the quiz and answers to the Mystery Case in the final published version. There are also links to other resident and fellow resources on the Neurology website and at AAN. We will now have the ability to print one RFS article in every print issue of Neurology and there is a new "Resident and Fellow Rounds" commentary written monthly by the RFS section editors that provides summaries of the RFS articles published with each issue. The RFS editorial team members are proud of the additional exposure through print distribution and expect that this will undoubtedly encourage the continued submission of high-quality manuscripts.

Neurology recognizes that the future of the journal, and the future of the field of neurology itself, depends on the interest and commitment of its readers and writers. This journal is one of the most important records of our profession, and current trainees are the profession's most valuable resource. Accordingly, the RFS is strongly supported by Neurology's current Editor-in-Chief Robert A. Gross, Executive Editor Patty Baskin, editorial staff, the AAN, and the publishers Wolters Kluwer. In particular, staff members Kathy Pieper and Robert Withrow have provided continual assistance and encouragement without which the section could not have survived. We welcome submission of manuscripts for the Resident & Fellow Section, and author instructions can be found at Neurology.org. Papers submitted for this section will undergo the same thorough peer review process as all Neurology submissions, and it is anticipated they will reflect the same high level of quality. It is further expected that manuscripts published in the section will carry the same academic weight, whether on-line or in print, as papers published elsewhere in Neurology. We also continue to welcome input from our readers, including program directors and other educators, on features that will be most valuable.

Questions and comments should be addressed to John Millichap, Roy Strowd, or Kathy Pieper at rfsection@neurology.org. We hope you enjoy this year's edition of the Highlights of the RFS!

John J. Millichap, MD, Section Editor, Resident and Fellow Section
Roy Strowd, MD, Deputy Section Editor, Resident and Fellow Section
Kathleen M. Pieper, Senior Managing Editor
Top 10 Ways for Program Directors to Use the Neurology Resident & Fellow Section
Ilena George, John J. Millichap, Roy E. Strowd

Visit the Resident & Fellow Section (RFS) website at Neurology.org/residents_fellows to access the features below:

1. The “Clinical Reasoning” subsection presents clinical cases with valuable teaching points. The cases feature either unusual presentations of common diseases, or rare disease entities. The goal is to work through the case step-by-step, focusing on the patient presentation, exam, and diagnostic investigations. This subsection can be the basis for an educational conference, a morning report, or can be a great starting point for incoming residents to hone their neurologic skills. In addition, the RFS has published a book consisting of “Clinical Reasoning” highlights, available as a free download at the website.

2. The “Mystery Case” subsection features a case with an undisclosed diagnosis and asks readers a few multiple-choice questions to identify the relevant pathology; the case is also featured on our Facebook page. Residency programs are invited to incorporate these into their curricula and join in the friendly mystery case competition. Respondents can track their performance over time and compare their answers with others online.

3. Each “Teaching NeuroImage” has a supplemental PowerPoint slide set available for download from the Neurology website. These can be used for group presentations or for a rapid review of illustrative or unique imaging findings. Video submissions for “Teaching Video NeuroImage” are also welcome and have expanded the range of phenomena demonstrated in this subsection.

4. “Journal Club” articles provide critical appraisals of recent articles published in Neurology with a focus on research methodology. The format is ideal for guiding discussions at Journal Club meetings.

5. The “Emerging Subspecialties in Neurology” subsection offers valuable new ideas and viewpoints for residents considering different career options. The RFS website also provides a link to the AAN Fellowship Directory.

6. The “E-Pearls” subsection, similar to “Teaching NeuroImages,” offers succinct learning points about a neurological presentation, which is ideal for rapid review. These are also highlighted via email to RFS Synapse community members.

7. The “Right Brain” subsection allows residents to exercise their “write” brain by composing narratives, poems, or using other creative means of expression. Since 2017, winning entry of the Consortium of Neurology Residents and Fellows Essay Contest has been published in this section.

8. The “Education Research” subsection reports high-quality research on educational topics, including surveys of program directors and residents, as well as studies on educational interventions. Program directors and residents alike will enjoy the novel ways residents find to improve education in residency and beyond. These articles are also a helpful resource for rising chief residents who are exploring new approaches to resident education.

9. Many residents are interested in scholarly activities but may not know how to start. Program directors can help residents get involved by encouraging them to write for the RFS! Refer to the “Call for Authors” page on the website for ideas to jump-start the writing process. All published articles are considered for the Annual Resident & Fellow Writing Award.

10. Follow the RFS on Facebook: Join our group entitled “American Academy of Neurology Residents and Fellows” and check out our new blog on the website above. For further digital access to RFS content, download the Neurology app onto your iPad/iPhone®, listen to the weekly Neurology podcast, and follow Neurology Twitter for updates.

Help spread the word!
Neurology Resident & Fellow Section Writing Award

The Winners of the 2018 Award Are:

Sheena Chew, MD, Ivana Vodopivec, MD, PhD, and Aaron L. Berkowitz, MD, PhD

For their article: Clinical Reasoning: An 82-year-old man with worsening gait

See page 13 of this Highlights book.

The Neurology Resident & Fellow Section Writing Award is intended to recognize the extraordinary writing abilities of those currently in training in neurology. Eligible manuscripts will include any submitted to and published in the Neurology Resident & Fellow Section, whether online or in print. Submissions on any topic of interest to trainees and in any subcategory of the section will be eligible. The main criteria for selection will be educational value, novelty, depth of exposition, and clarity of writing. At least one author of the manuscript must be currently in a neurology residency program or in fellowship training in one of the neurological subspecialties. All authors will be considered equal recipients of the award in order to recognize and encourage collaborative work among trainees. The next award will be announced in early 2019 and will be awarded for a paper published in 2018.

No formal application process is required. All manuscripts submitted to the section will be considered. Manuscripts should be submitted online at NPub.org/submit. Please direct any questions to rfsection@neurology.org.

PAST RECIPIENTS

2017 Award Winner
For their article: Pearls & Oy-sters: Episodic ataxia type 2: Case report and review of the literature
Elan L. Guterman, MD, Brian Yurgionas, MD, MS, and Alexandra B. Nelson, MD, PhD
Neurology June 7, 2016, 86:23 e239-e241

2016 Award Winner
Emerging Subspecialties in Neurology: Telestroke and teleneurology
Sunil A. Mutgi, MD; Alicia M. Zha, MD, and Reza Behrouz DO
Neurology June 2, 2015, 84:22 e191-e193

2015 Award Winner
Clinical Reasoning: An unusual cause of transverse myelitis?
Pavan Bhargava, MD, and Rodger J. Elble, MD, PhD
Neurology February 11, 2014, 82: e46-e50

2014 Award Winner
Right Brain: A reading specialist with alexia without agraphia: Teacher interrupted
Jason Cuomo, MA; Murray Flaster, MD, PhD; and José Biller, MD
Neurology January 7, 2014, 82:e5-e7

2013 Award Winner
Clinical Reasoning: A 55-year-old woman with vertigo: A dizzying conundrum
Daniel R. Gold and Stephen G. Reich
October 23, 2012, 79:e146-e152

2012 Award Winner
Child Neurology: Brachial plexus birth injury: What every neurologist needs to know
Christina B. Pham, Johannes R. Kratz, Angie C. Jelin, and Amy Gelfand
Neurology August 16, 2011, 77:695-697

2011 Award Winner
Right Brain: We were all once ‘fixed and dilated’
Amy Gelfand, MD
November 16, 2010, 75: 1851-1852
August 21, 2017: MELAS

MELAS (“Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes”) is one of the most common mitochondrial disorders. The 2012 Japanese diagnostic criteria are divided into category A: seizures, headaches with vomiting, hemiplegia, cortical blindness, and acute focal lesions in neuroimaging; and category B: high plasma or cerebrospinal fluid (CSF) lactate, mitochondrial abnormalities in muscle biopsy and a MELAS-related gene mutation. For a definitive diagnosis of MELAS the patient should meet at least two category A and two category B criteria.1 Stroke-like episodes are secondary to metabolic infarcts due to defects in neuronal metabolism. They do not follow vascular territories, and they show a predilection for the parietal, temporal and occipital lobes. The affected areas have elevated lactate peaks on MR spectroscopy and diffusion restriction on MRI. More than 80% of patients have the m.3243A>G mutation in the mitochondrial tRNA gene.2 Treatment involves intravenous L-arginine infusion during the acute attack, and oral arginine interictally, which help reverse and prevent attacks respectively.2 Other supplements (coenzyme Q10, citrulline, idebenone, edaravone, multivitamins) are also used to improve mitochondrial respiratory complex function and reduce levels of reactive oxygen species. Drugs that cause mitochondrial dysfunction should be avoided, particularly valproic acid.1

References

Submitted by Alfonso Sebastian López-Chiriboga, MD - Department of Neurology, Mayo Clinic.
Dr. López-Chiriboga reports no disclosures.

November 6, 2017: Hemiconvulsion hemiplegia epilepsy syndrome (HHE)

HHE is an unusual consequence of focal febrile status epilepticus in children younger than four years of age. It is characterized by prolonged unilateral clonic seizures followed by transient or permanent ipsilateral hemiplegia. HHE can be idiopathic, occurring in healthy children in the setting of fever and extracranial infection. Or it can be symptomatic, as a seizure due to etiologies such as intracranial infection, head injury or brain lesions. Early radiological findings include unilateral subcortical white matter edema with subsequent hemiatrophy within weeks to months. Anti-edema agents like mannitol or hypertonic saline and N-methyl-D-aspartic acid glutamate receptor antagonists during the time of hemiconvulsions may help to stop neuronal injury.

References

Submitted by Akilandeswari Aravindhan, MBBS, and Dr. Aravindhan Veerapandiyan, MBBS—Rutgers University, New Jersey Medical School.
Dr. Aravindhan and Dr. Veerapandiyan report no disclosures.
Child Neurology

The Child Neurology section in the Resident & Fellow Section of *Neurology* focuses on contemporary educational issues in child neurology. The goal of the section is to provide up-to-date reviews on important topics in child neurology that are relevant to all neurologists, both adult and child, particularly those still in their training. Examples include management of acute stroke in children, childhood demyelinating disease, neuroimaging in metabolic disorders, and the neurobiology of autism. Each piece will begin with a patient case, followed by a brief discussion about the differential diagnosis and a detailed discussion about the topic of focus. Submissions are welcome from residents and fellows in either child or adult neurology. Ideally, submissions will include the patient case as well as the discussion, but submission of timely review articles without an accompanying case will also be considered. In this situation, the editors of this section may supply an appropriate patient case.
A 3-year-old girl presented with 4 days of progressive bilateral vision loss. Medical history included presumed autoimmune hepatitis at 6 months of age, when she had an extensive evaluation including hepatitis A immunoglobulin G (IgG) detected in her serum, thought to represent maternal antibodies. Liver biopsy suggested autoimmune hepatitis and she was treated with oral prednisolone 2 mg daily for 2 weeks and remained on maintenance 1 mg daily. Family and social histories were unremarkable.

Neurologic examination demonstrated severely decreased central vision in both eyes; pupils were slowly reactive to light without relative afferent pupillary defect. She had a left Babinski sign. The remaining general and neurologic examinations were normal, including funduscropy.

MRI brain, orbits, and spine with contrast demonstrated bilateral optic neuritis (ON; figure) and no other lesions.

CSF contained 0 nucleated cells/μL, 1 erythrocyte/μL, glucose 47, protein 30, no oligoclonal bands, and elevated IgG index at 0.81 (0.28–0.66). The patient had normal folate, cyanocobalamin, and sedimentation rate/C-reactive protein, and was anti-nuclear antibody (ANA)-positive at 1:640 with a nucleolar pattern; other rheumatologic antibodies were absent. Serum aquaporin-4 IgG (AQP4-IgG) was pending at the time of treatment.

The patient was treated empirically for neuromyelitis optica (NMO) spectrum disorder (NMOSD) with plasma exchange (PLEX) and 20 mg/kg/d IV methylprednisolone (IVMP) on the day of presentation. With 5 sessions of PLEX/IVMP, her vision improved significantly. She was discharged with oral prednisone and serum AQP4-IgG returned positive at 73 units/mL. She was given rituximab 375 mg/m² on days 1 and 15, and then every 3 months thereafter. Her vision subjectively improved somewhat after her first cycle of rituximab.

DISCUSSION Eugène Devic first coined “neuromyelitis optica” in 1894 while describing a novel syndrome of acute myelitis and ON. Discovery of the pathogenic AQP4-IgG led to the development of international diagnostic criteria that include AQP4-IgG status. Clinical features include ON (severe/bilateral), longitudinally extensive transverse myelitis (≥3 vertebral segments), and area postrema syndrome (intractable hiccups, nausea/vomiting). Brainstem and diencephalic syndromes such as narcolepsy/hypersomnolence and endocrine dysfunction have also been recognized in NMOSD. It is important to distinguish NMOSD from multiple sclerosis (MS) and other disorders as treatment differs among these and prompt treatment is important for minimizing disability.

The differential diagnosis of ON has recently been reviewed and will not be covered in detail. Infectious etiologies should be considered when there are infectious signs/symptoms or highly inflamed CSF. Deficiencies in cyanocobalamin, folate, and copper should be considered when there is bilateral optic neuropathy, especially in an at-risk patient (e.g., malabsorption syndromes, gastrointestinal surgery). The clinical features and subacute–progressive time course of NMOSD and other demyelinating conditions help to distinguish them from other diagnoses, which may tend to be more hyperacute (vascular) or chronic (genetic/nutritional).

Clinical features of NMOSD in children. In one analysis of children with NMOSD, the most common presenting features included visual, motor, and constitutional syndromes. In the largest report of children with NMO, 83% and 78% of children with AQP4-IgG had at least one episode of ON or transverse myelitis, respectively, while 45% had other symptoms such as encephalopathy, seizures, ophthalmoplegia, ataxia, or area postrema syndrome. Children with NMOSD were older than those with acute disseminated encephalomyelitis (ADEM) (mean 10–12 vs 5 years), but approximately the same age as those with MS (13 years). Female patients and non-Caucasians are overrepresented in NMOSD. NMOSD is associated with additional autoimmunity, with 42% and 76% of patients with other autoimmune diagnoses or...
autoantibodies, respectively. Sixty-four percent have a positive ANA, as in our case. There is one other case of autoimmune hepatitis associated with NMO reported in the literature.

**Imaging features of NMOSD in children.** MRI with gadolinium is the imaging modality of choice for evaluating possible demyelinating disease, although there are no definitive radiologic criteria for NMO in children. MRI brain, orbits, and cervical ± thoracic spinal cord should be imaged as clinically indicated. Among 56 patients with MRI data included in one study, 56% had brain parenchymal abnormalities and 34% had optic nerve contrast enhancement; 5 had involvement of the chiasm and 1 had bilateral ON. ON caused by NMOSD is more likely to be clinically severe, bilateral, and longitudinally extensive, and to involve the optic chiasm, compared to other causes of ON. Features that help distinguish NMOSD myelitis from MS include longitudinally extensive (≥3 spinal segments) myelitis involving the central cord with >50% of the crosssectional area, compared to the shorter, smaller, and longer lesions seen in MS. Brain lesions are common in pediatric NMOSD and may overlap with MS or ADEM. NMOSD lesions tend to be periependymal T2 hyperintense lesions predominantly. Periventricular NMOSD lesions tend to be longer than the Dawson fingers seen in MS, which are usually shorter and confined to the pericallosum. Lesions in the corpus callosum occur in NMOSD, where they are often large and follow the ependymal lining, while those seen in MS tend to be smaller, ovoid, or flame-shaped and oriented radially to the ventricles. Extensive and confluent predominantly white matter hemispheric lesions, which may be associated with encephalopathy, can make it difficult to distinguish NMOSD from ADEM. In that setting, laboratory features, particularly the presence of AQP4-IgG, can be critical to the diagnosis.

**Laboratory features of NMOSD in children.** Roughly 65% of children with NMOSD tested positive for AQP4-IgG, rates similar to those observed in adults with NMOSD, but seropositivity may occur up to 4–5 years after onset. Testing for AQP4-IgG is the
serum, which is the source recommended by the Mayo Clinic laboratory. In ON from NMOSD, the CSF may appear bland, while during an episode of myelitis, CSF may be highly inflamed, with pleocytosis >100 cells/µL, commonly with neutrophils or eosinophils. Oligoclonal bands are observed in roughly 25% of patients with NMOSD. This is contrasted with CSF in MS, which commonly contains oligoclonal bands (90%) and only rarely is pleocytosis >50, typically lymphocytic. CSF studies in children with ADEM are variable and often nondiagnostic; however, oligoclonal bands are only rarely present. Children with features of NMOSD but with negative serum AQP4-IgG should have CSF AQP4-IgG testing and may also be tested for myelin-oligodendrocyte glycoprotein antibodies (in the United States, only available through research laboratories). AQP4-IgG may appear up to 4 years after disease onset, and sequential testing should be employed for initially seronegative patients.

**Diagnostic criteria in children.** The Wingerchuk 2006 criteria were 49% sensitive for a diagnosis of pediatric NMO, while the 2015 updated international panel for NMO diagnosis criteria, which allowed for diagnosis after one attack and the presence of AQP4-IgG, were 97% sensitive and can be applied to children. This is in part due to the lower lesion accrual in pediatric NMO.

**Treatment of NMOSD in children.** In contrast to MS, in which disability is driven primarily by progressive disease and there is relatively good recovery after acute exacerbations, in NMOSD, acute exacerbations can be severe with little recovery and drive virtually all of the disability. In addition, 93%–95% of children with NMOSD have relapsing disease, and there is some evidence that acute exacerbations respond more favorably when the patient is on preventative medication. Therefore, prompt recognition and initiation of acute abortive therapy and preventative medication is critical. Some disease-modifying therapies used in MS (including interferons, fingolimod, and natalizumab) are ineffective and may worsen NMOSD. No randomized controlled trials have been conducted in adult or pediatric NMOSD; therefore, all treatments are considered off-label and based on available literature and expert recommendations.

**Acute treatment.** Acute exacerbations are commonly treated with IVMP (in children 20 mg/kg/d for 5 days), an approach extrapolated from data on treating other immune-mediated neurologic conditions. We advocate for urgent PLEX as a first-line therapy for NMOSD exacerbations based on evidence demonstrating improved outcomes in patients treated with PLEX and IVMP compared to IVMP alone. At Vanderbilt Children’s Hospital, we exchange 1.5 volumes of plasma 5 times over 5–8 days. Complications are uncommon in experienced centers, but include those related to the central line, electrolyte abnormalities, and coagulopathy associated with the exchange process and transfusion-related complications. IV immunoglobulin may be beneficial and can be considered when there is a poor response to steroids and contraindication to PLEX exists. Children with NMOSD should be given a prednisone taper over several months.

**Preventative therapy.** The most common preventative agents include azathioprine, prednisone, mycophenolate mofetil, and rituximab. There is evidence to support the use of rituximab or mycophenolate over azathioprine. The same strategies used to treat adults with NMOSD have been applied to children, and results appear comparable. Studies intended to assist with the dosing and monitoring of rituximab for pediatric NMOSD have begun to emerge in the literature.

As recently demonstrated, the updated international panel for NMO diagnosis criteria are sensitive for the diagnosis of NMOSD in children. Prompt recognition and treatment of exacerbations followed by initiation of preventative agents are critical for minimizing disability. Strong consideration should be given to treating acute exacerbations with urgent PLEX in addition to IVMP, which appears to be more effective than IVMP alone.

**AUTHOR CONTRIBUTIONS**

Michael J. Bradshaw: treating clinician, literature review, clinical review, imaging review, manuscript preparation, editing. NgocHanh Vu: manuscript review, editing. Tracy E. Hunley: treating clinician, manuscript review. Tanuja Chitnis: manuscript review, editing.

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**REFERENCES**


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Clinical Reasoning

Clinical Reasoning focuses on case presentations with the aim of developing clinical reasoning skills among trainees. Appropriate cases for publication would include uncommon presentations of common neurological disorders and also typical presentations of more exotic disorders. The emphasis of the case presentation should be on generating a sound, thorough differential diagnosis; logically arriving at the correct diagnosis; and thoughtfully discussing the teaching-points of the case. Cases discussed in the section should utilize data presented serially in two to four segments that could be opened sequentially by the reader, allowing them to challenge themselves by thinking through the differential diagnosis or treatment options at each step. The manuscript should indicate where each break would occur, with specific questions for the reader to consider as they work their way through the case. The final section should provide the experienced clinician’s discussion (or resident author’s literature review). Ideally the individual sections will also include visually presented data, such as radiology, EEG, EMG, or other studies. See published samples as examples.
Clinical Reasoning: An 82-year-old man with worsening gait

**SECTION 1**

An 82-year-old man with hypothyroidism presented with difficulty walking.

One year prior to presentation, he noticed that his legs occasionally “froze” when initiating walking. His gait progressively worsened over the year. He developed balance difficulty, tripping and falling twice without loss of consciousness. In the 4 months prior to presentation, he started using a cane, a rolling walker, then a wheelchair. He reported occasional neck and left leg cramps. He denied bowel or bladder symptoms.

The patient was previously healthy, playing competitive sports at the national level into his late 70s. His only medication was levothyroxine.

**Question for consideration:**
1. What examination findings would help to localize the etiology of his abnormal gait?

**SECTION 2**

Potential explanations for altered consciousness and tremors include intoxications (lithium, serotonergic, or antiepileptic drugs) and alcohol withdrawal. The tremor described here has the typical characteristics of a lithium tremor. These symptoms, in combination with elevated lithium levels led to a diagnosis of severe lithium neurotoxicity due to hypovolemia-induced renal failure. Since the excretion of lithium is almost uniformly renal, acute lithium toxicity may be initiated by a loss of renal function. Patients with lithium intoxication often develop gastrointestinal symptoms, e.g., nausea and vomiting. If these symptoms are severe, dehydration and decreased renal function may develop. This impairs the ability to excrete lithium and exacerbates lithium toxicity. Therapeutic intervention should focus on rehydration and the removal of lithium from the body. Restoration of electrolyte and water balance by rehydration in hypovolemic patients with lithium toxicity is mandatory to maintain or restore kidney function and maximize lithium clearance. Removal of lithium should be achieved by discontinuation of the drug as well as extracorporeal removal by means of hemodialysis or continuous veno-venous hemofiltration (CVVH). Lithium is readily dialyzable since it is nonprotein bound and has a low molecular weight and a small volume of distribution. Usually one session of hemodialysis or 24 hours of CVVH is sufficient, although some experts advise to continue dialysis after normal (<1 mmol/L) levels of lithium have been achieved to prevent a rebound effect.

In our patient, treatment was initiated with rehydration as well as CVVH and the patient was admitted to our intensive care unit (ICU). CVVH was continued for 24 hours, which resulted in a decrease of lithium levels toward therapeutic levels. However, severe lethargy as well as neurologic sequelae persisted for 14 days despite normalization of lithium levels.

**Question for consideration:**
1. Should a different diagnosis be considered in view of the persistence of neurologic symptoms?
SECTION 3
Neurologic complications of lithium intoxication usually develop later in the clinical course because of the relatively slow absorption in the CNS. Furthermore, they may persist despite removal of lithium by hemodialysis or hemofiltration. This “syndrome of irreversible lithium effectuated neurotoxicity” (SILENT) is characterized by prolonged neurologic and neuropsychiatric sequelae, which may persist for months. Demyelination at multiple sites in the CNS has been suggested to be the cause and can sometimes be observed on MRIs as focal white matter abnormalities.\(^3\,^4\) In our patient, in addition to her neurologic symptoms, episodic symptomatic bradycardias and atrioventricular (AV) blocks associated with hypotension were observed during her stay at the ICU. Upon careful analysis, we observed a close relationship of bradycardias with swallowing. The patient denied ever having symptomatic bradycardias or presyncope complaints when swallowing before the current episode of lithium intoxication. A representative ECG after swallowing is shown in the figure; also see the video on the Neurology\(^{®}\) Web site at Neurology.org (which was recorded relatively late in the clinical course). These bradycardias persisted during the first week of admission but eventually diminished and disappeared. After 2 weeks of admission, her neurologic symptoms slowly improved as well and she was discharged toward a psychiatric care facility for rehabilitation, reinstitution, and optimization of medical therapy for her bipolar disorder.

Questions for consideration:
1. What is the phenomenon observed in the figure and the video?
2. What is the presumed pathophysiology of this phenomenon and what is its relation to lithium intoxication?

Figure Bradycardia and atrioventricular block during swallowing

A real-time ECG recording during swallowing is shown. Initial normal sinus rhythm changes after swallowing, and bradycardia as well as high-degree atrioventricular block are observed.
Our patient had episodes of swallow-induced transient bradycardia. As bradycardia was not severe enough to cause loss of consciousness, these episodes do not fulfill the criteria for syncope. Nonetheless, episodes of swallow-induced bradycardia are characteristic for “swallow syncope,” a rare syndrome that belongs to the reflex syncope syndromes. The pathophysiology of swallow syncope is incompletely understood but likely involves a vagal reflex that is initiated by activation of the glossopharyngeal nerve during swallowing. Efferent impulses lead to the sinoatrial node (right vagus nerve) or the AV node (left vagus nerve) and may lead to various types of paroxysmal bradycardias and reduction of cardiac output. The importance of vagal pathways in this reflex is stressed by studies in which pretreatment with atropine or other anticholinergic drugs is effective in preventing swallow-induced bradycardia. A recent review of all 80 published cases of swallow syncope showed that the majority of cases (62%) had underlying cardiac or gastrointestinal disease, although a substantial minority of patients did not have any underlying pathology. Treatment of the syndrome may involve implantation of a permanent pacemaker. In patients in whom quality of life is severely affected by recurrent syncopal events, this treatment is usually effective.

DISCUSSION Herein, we report a case of a patient who had been chronically treated with lithium who developed severe neurologic as well as cardiac symptoms due to an intoxication of lithium, which was caused by prerenal kidney insufficiency-related reduced elimination of lithium. Lithium salts have been used for the treatment of psychosis and bipolar disorder since the 19th century. Although effective, it has a narrow therapeutic index. This is illustrated by the fact that a majority of patients chronically treated with lithium experience at least one episode of toxicity during their course of treatment. Patients may be relatively asymptomatic despite very high serum concentrations, and severe clinical toxicity may develop despite lithium concentrations in the therapeutic range. Therefore, the diagnosis and treatment of this syndrome should rely on a combination of clinical symptoms as well as drug levels.

Despite rapid normalization of plasma lithium levels, neurologic symptoms persisted for several weeks, which is consistent with the SILENT syndrome as discussed above. Potential neurologic symptoms include lethargy and coma, ataxia, confusion or agitation, and neuromuscular excitability. In addition to neurologic symptoms, she developed cardiac toxicity: she presented with a markedly prolonged QTc time, which did not lead to rhythm disturbances initially and normalized rapidly after plasma lithium levels were corrected. Of note, however, during her stay at the ICU, she developed symptomatic sinus node bradycardias as well as AV blocks that were provoked by swallowing. Cardiac toxicity may cause changes in the ECG. Although arrhythmias are rare, prolonged QTc intervals and bradycardia have been reported. Whereas swallow-induced bradycardia has been described previously, provocation of this syndrome by lithium toxicity has not. Lithium exerts its actions through the alteration of sodium transport in neurons, which increases intraneuronal metabolism and reduces stores of catecholamines. In the heart, lithium is a potent blocker of cardiac sodium channels. This lithium-related blockade of sodium channels can unmask conduction abnormalities in the heart such as conduction delays as well as Brugada syndrome although other mechanisms of lithium-associated bradycardias have been described as well. Plans were made to perform extensive autonomic nervous system tests in our patient to evaluate the effects of vagal maneuvers on her symptoms and heart, but unfortunately these were hampered by her persistent neurologic and psychiatric symptoms. By the time her neuropsychiatric status improved, her episodes of swallow syncope had resolved completely. Finally, we aimed to exclude whether genetic defects in ion channels contributed to the observed clinical phenomena. Recent molecular insights have defined a molecular basis for sinoatrial and AV node dysfunctions and several mutations in the genes encoding for cardiac sodium channels have been described that contribute to these dysfunctions. To analyze whether such mutations may have had a role in our patient’s symptoms, we performed genetic testing of our patient and tested for mutations in 48 genes (next-generation sequencing arrhythmia panel, http://amsterdamgenomedx.com) that are associated with arrhythmias but were unable to find genetic polymorphisms that predispose to arrhythmias in this specific case. We postulate that lithium provoked episodes of swallow-induced bradycardia in our patient due to the combined effects of swallowing-induced vagal efferent activity and an increased susceptibility to bradycardia caused by lithium.

AUTHOR CONTRIBUTIONS Dr. van Westdoo: concept and design of the report, data accrual, wrote the manuscript. Dr. Barge-Schaapveld: analysis of genetics, critical revision of the manuscript for important intellectual content. Dr. Bikker: performed DNA analysis, critical revision of the manuscript for important intellectual content. Dr. van Noorden: critical revision of the manuscript for important intellectual content. Dr. Tannemaat: concept and design of the report, data accrual, cowrote the manuscript.

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- You can include a maximum of five authors (including yourself)
Education Research

As the central mission of *Neurology*, education is a top priority. This is a section for interventional educational studies, as well as more traditional educational research, such as surveys. This section will examine the way neurologists not only practice, but also the way we teach and approach education. Neurologists have traditionally been respected, perhaps above all other specialties, for their scholarship and teaching. Educational issues will therefore continue to be at the center of the mission of *Neurology*.
Education Research: Positive effect of scheduled faculty modeling on clerkship student bedside skills exposure and learning

ABSTRACT

Objective: To evaluate the effect of scheduled bedside skills modeling for third-year medical students on their neurology clerkship.

Methods: During the 2012–2014 academic years, 56 third-year medical students participated in a curricular pilot program involving a scheduled bedside skills modeling experience during the first week of their neurology clerkship, whereas 131 students underwent the typical rotation. The experience consisted of observing a faculty member conduct a comprehensive encounter on a new outpatient. To promote active learning, students were provided an observation guide to document questions and observations. An anonymous survey was conducted at the end of each clerkship block assessing student exposure to bedside skills modeling. Using qualitative thematic analysis, observation guide statements were transcribed and coded into emergent learning themes.

Results: A total of 57.4% (95% confidence interval [CI] 43.3%–71.5%) of students in the modeling group reported observing both a comprehensive history and neurologic examination vs 37.5% (95% CI 28.2%–46.8%) in the nonmodeling groups (p = 0.023). A total of 253 observation statements were transcribed and coded from the observation guides. The most common learning themes included (1) strategies for performing a neurologic examination, (2) techniques for eliciting a neurologic history, and (3) importance of detail and thoroughness of the history and examination.

Conclusions: Our study demonstrated that there was a significant increase in structured observation by students of neurologic bedside skills with the inclusion of a scheduled modeling experience, and we provide a qualitative description of the most common learning themes associated with this experience. Neurology® 2017;88:e236–e239

GLOSSARY

CI = confidence interval.

In the modern medical era, bedside skills have become devalued with increased reliance on medical technological advances and the electronic health record. Numerous editorial and opinion articles have been published in recent years highlighting the decline in bedside skills education for medical trainees and the effect of this on patient care.1–4 Despite this knowledge, it is currently estimated that only 8%–19% of learning is done in the presence of the patient.5 Barriers to bedside teaching include devaluation of teaching and inadequate faculty development to promote bedside teaching skills among faculty.6–7 Modeling of clinical encounters has been shown to improve both physical examination and procedural skills, and can be effective for teaching humanism and professionalism values.8–10

The aim of this study was to evaluate whether a scheduled modeling experience for third-year medical students starting their neurology clerkship increased overall student exposure to clinical skills modeling during the clerkship. In addition, we intended to discover using qualitative thematic analysis what specific learning points were acquired during the experience.

METHODS Participants. During the 2012–2014 academic years, a portion of University of Rochester School of Medicine and Dentistry third-year neurology clerks participated in a pilot aimed at improving bedside learning and instruction. During the first academic year, students in 4 out of 8 clerkship blocks (56 total) participated in a scheduled modeling experience, whereas students in the remaining blocks underwent the typical rotation (131 total). This is a retrospective study done to analyze the usefulness of this
bedside modeling pilot. It was evaluated by the University of Rochester Research Subjects Review Board, which determined that it met federal and University criteria for exemption.

**Modeling experience.** For the modeling experience, students were scheduled to observe a clinical encounter during the first week of the clerkship. This consisted of a 1-hour session with a faculty member in the outpatient clinic setting. During this time, the student observed the neurologist conduct a comprehensive history and neurologic examination on a new patient, followed by an opportunity for questions and debriefing. Students were supplied with an observation guide that detailed the elements of the history and neurologic examination, included a checklist for each element, and allowed space for written observations and questions (figure e-1 at Neurology.org). Faculty were recruited to model these encounters via e-mail on a voluntary basis. They were provided with a preceptor guide as training that included a general description of the procedure to follow as well as the major learning goals for the student.

**Data analysis and student survey.** At the conclusion of each clerkship block, students completed an anonymous survey meant in part to assess their exposure to modeling experiences during the clerkship. The survey was delivered on the last day of their 4-week rotation. The survey was developed by one of the study authors (R.T.S.) for the purpose of assessing the curricular change, and piloted during the first clerkship block of the trial period. Students were asked about their ability to observe a faculty member perform bedside skills (for definitions, see survey questions in figure e-2). The proportion of students reporting observation of a comprehensive history or comprehensive examination was calculated in the 2 groups, and their difference compared using a 2-sample z test, with a 2-tailed \( \alpha \) of 0.05.

Qualitative thematic analysis was undertaken to examine patterns of student learning during the experience. To conduct this analysis, the observation guides were collected, deidentified, and written student comments/questions were transcribed. Subsequently, 2 members of the research team (R.T.S., T.T.) independently reviewed the transcribed statements and coded emergent learning themes and subthemes through their reading of the statements. Since this was a retrospective study, a set number of statements were available and saturation of themes could not be assumed. In a consensus-building meeting, the 2 coders discussed their independent themes, and consolidated and refined them through discussion to create the final coding.

**RESULTS** The end-of-rotation survey had an overall response rate of 81% (84% for modeling group; 79% for nonmodeling group). Of the 47 students in the modeling group who responded to the survey, 57.4% (95% confidence interval [CI] 43.3%–71.5%; \( n = 27 \)) reported that they successfully observed a comprehensive encounter (defined as both a comprehensive history and complete neurologic examination). In contrast, 37.5% (95% CI 28.2%–46.8%; \( n = 39 \)) of the 104 students in the nonmodeling group who completed the survey reported observing a comprehensive encounter \( (p = 0.023) \). The remainder of our survey data that compare student ability to observe the history and examination are presented in table e-1.

A total of 43 completed observation guides were collected from the 56 students who participated in the modeling experiences. A total of 253 observation statements were transcribed and coded from the returned observation guides, and 5 major learning themes as well as numerous subthemes were identified (table 1). The following serve as exemplar statements from each category.

**Strategies/techniques for performing a neurologic examination.**

“[I] learned to stabilize the joint for more effective strength testing.”

<table>
<thead>
<tr>
<th>Theme</th>
<th>Total statements (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strategies/techniques for performing a neurologic examination</td>
<td>103 (40.7)</td>
</tr>
<tr>
<td>Technique of a specific examination component (e.g., cranial nerve, reflexes)</td>
<td>75</td>
</tr>
<tr>
<td>Neurologic examination of the pediatric patient</td>
<td>28</td>
</tr>
<tr>
<td>Evaluation when psychogenic etiology suspected</td>
<td>4</td>
</tr>
<tr>
<td>Evaluation when acute stroke suspected</td>
<td>3</td>
</tr>
<tr>
<td>Techniques for eliciting a neurologic history</td>
<td>73 (28.9)</td>
</tr>
<tr>
<td>Eliciting/clarifying history</td>
<td>28</td>
</tr>
<tr>
<td>Eliciting pediatric history</td>
<td>17</td>
</tr>
<tr>
<td>Open-ended questioning</td>
<td>9</td>
</tr>
<tr>
<td>Directing history based on chief complaint</td>
<td>7</td>
</tr>
<tr>
<td>Role of records/prewritten questionnaires in history-taking</td>
<td>5</td>
</tr>
<tr>
<td>Involving all individuals present</td>
<td>4</td>
</tr>
<tr>
<td>Summarizing information</td>
<td>3</td>
</tr>
<tr>
<td>Importance of detail, thoroughness of history and examination</td>
<td>45 (18)</td>
</tr>
<tr>
<td>Thorough/time spent</td>
<td>18</td>
</tr>
<tr>
<td>Importance of including all sections of history and establishing important details</td>
<td>14</td>
</tr>
<tr>
<td>Necessity for detailed examination</td>
<td>13</td>
</tr>
<tr>
<td>Importance of connecting and communicating with the patient and family</td>
<td>19 (7.5)</td>
</tr>
<tr>
<td>Communication skills</td>
<td>9</td>
</tr>
<tr>
<td>Showing empathy and compassion</td>
<td>7</td>
</tr>
<tr>
<td>Family-centered communication</td>
<td>3</td>
</tr>
<tr>
<td>Strategies for effective flow of the encounter</td>
<td>13 (5.1)</td>
</tr>
<tr>
<td>Flow and organization of examination</td>
<td>8</td>
</tr>
<tr>
<td>Flow of history-taking</td>
<td>5</td>
</tr>
</tbody>
</table>
“[I learned how to] assess for Hoover sign to help distinguish [poor] effort from true weakness.”

“Must do [limb dysmetria testing] in full extension or won’t accurately test.”

Techniques for eliciting a neurologic history.

“[The attending] directed [the] HPI and history of weakness away from [their] previous health care visits.”

“[The attending] avoids trying to give synonyms for sensations, instead asks ‘how would you describe it?”

“[The attending] puts a lot of emphasis on understanding [the] patient’s baseline mental status and ADLs.”

Importance of detail and thoroughness of the history and examination.

“[The attending] spent approximately 75% of visit on HPI, at least ≥30 minutes!”

Importance of connecting and communicating with the patient and family.

“[The attending] establishes great rapport by involving all members of family present (allowed all family members to feel like part of the plan).”

“Explained diagnosis and plan, discussed treatment and side effects [in such a way so] the patient felt heard.”

Strategies for effective flow of the encounter.

“[I was] struck by the flow of the exam—[the physician] had her distinctive approach to the exam, organized to her preferences.”

DISCUSSION The main findings of this study are (1) the significant increase in students reporting observation of comprehensive neurologic bedside evaluations with the inclusion of a scheduled modeling experience in the neurology clerkship curriculum and (2) a qualitative description of the most common learning themes associated with such a modeling experience.

The survey data show that students who underwent the structured modeling blocks were significantly more likely to report having observed a comprehensive neurologic encounter (as opposed to problem-focused). There is no literature identifying the specific merits of modeling a comprehensive history and examination; however, there are theoretical benefits, including the ability to learn the flow of an efficient yet complete neurologic examination and the thoroughness and time spent by a neurologist obtaining a neurologic history and examining a new patient. These theoretical benefits are supported by their inclusion in our discovered learning themes. In addition, exposing the student to a comprehensive physical examination ensures that the student observes all elements during the clerkship. In addition to the opportunity to learn proper techniques for history-taking and examination, modeling is essential for teaching physician–patient communication skills and professionalism, and this pilot provided further opportunity for such learning.

Our qualitative analysis yielded various learning themes associated with the modeling experience. These results provided insight into the shared experiences of direct observation from the students’ perspective. This knowledge could help shape future formal modeling experiences, allowing us to make informed improvements to learning objectives and observation guides. For example, all students could be asked to complete an observation guide that includes listing examination techniques that were novel to them or applied to a specific disease state. It is difficult to assess the effect modeling may have had on the student’s ultimate neurologic bedside skills given the many clinical experiences throughout the clerkship. However, the results of our qualitative analysis are congruent with previous studies that have shown the effectiveness of live modeling experiences on acquiring procedural (including physical examination) and cognitive skills.

There were a few challenges that we identified to the incorporation of a scheduled modeling experience for neurology clerks, and the biggest difficulty was how to work the experience around clinic no-shows. There were several limitations to this study as well. The sample size of students who participated in the modeling experience was relatively small. In addition, this was a retrospective evaluation of an educational curricular change, and as such it is not clear that saturation of learning themes was reached. Another important consideration is that the student survey was not specifically validated. We were evaluating both the structured modeling experience as well as active learning with an observation guide, and could not separate these interventions in the analysis. As such, students participating in the scheduled modeling experience may have been more likely to recall observing a comprehensive encounter.

Future studies could include collecting qualitative data from students undergoing structured modeling on their perceptions of the importance of the history and examination, and how their knowledge, skills, or attitudes about clinical practice may have been affected by the experience. In addition, it would be worth examining the differences in learning themes between students observing a comprehensive vs problem-focused neurologic encounter to discover whether or not the former allows for more educational opportunities. Our study demonstrates the benefit of scheduling modeling encounters to increase
student exposure to observation of comprehensive neurologic bedside skills. In an era where the use of bedside teaching has diminished, the program helped bring learning back to the patient.

AUTHOR CONTRIBUTIONS
Robert Thompson Stone: design and conceptualization of the study, analysis and interpretation of the data, drafting and revising the manuscript. Trenton Tollefson: analysis and interpretation of the data, aided in drafting the manuscript. Ronald Epstein: conceptualization of the study, aided in drafting the manuscript. Ralph Jozefowicz: conceptualization of the study, aided in drafting the manuscript. Jonathan Mink: conceptualization of the study, aided in drafting the manuscript.

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DISCLOSURE
The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES

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Emerging Subspecialties in Neurology

These manuscripts will review the history and development of emerging subspecialties in neurology, including fields such as pain medicine, headache, neurocritical care, interventional neurology, and others. The focus should be on educating residents with a possible interest in this subspecialty. Those interested in writing these manuscripts should contact the Resident & Fellow Section editor before submission to inquire about the need for an article on a particular topic.
Emerging Subspecialties in Neurology: Autoimmune neurology

Autoimmune neurology is one of the most rapidly evolving fields in modern neurology. Autoantibodies that recognize nervous system self-antigens, including ion channels, receptors for neurotransmitters, and neuronal intrinsic and extrinsic proteins involved in synaptic transmission, are all recognized as targets of pathogenic autoantibodies. The accelerating rate of new antigen discovery in recent decades is impressive (figure). The diversity of neurologic presentations, the unique pathophysiology, and the complexity of treating these disorders justifies dedicated fellowship training to acquire the expertise needed to diagnose and optimally manage these patients. The requisite training is distinct from the classical exposure provided by traditional neuroimmunology fellowships that focus on multiple sclerosis. As a new subspecialty, autoimmune neurology intersects all neurologic subspecialties and other medical specialties, including but not limited to clinical immunology, infectious disease, rheumatology, gastroenterology, oncology, and psychiatry. While this article focuses on autoimmune neurology fellowships currently available in the United States, historically many current leaders in the field trained nationally and internationally under Dr. Jerome Posner, Dr. John Newsom-Davis, and Dr. John Trotter, to name a few of the pioneers.

HISTORICAL DEVELOPMENT Clinical training in autoimmune neurology was pioneered by Dr. Vanda Lennon, who established the first formal autoimmune neurology fellowship program in 2005 at the Mayo Clinic, Rochester, Minnesota. Dr. Sean Pittock, one of her early clinical fellows, was co-director of the program. Antibody-mediated neurologic diseases have been recognized since the mid-1970s.

Prior to the last 4 decades of authenticated autoimmune serologic testing, recognition and diagnosis of autoimmune neurologic disorders in clinical practice was limited, and few effective treatments were available. There was also a widely held belief that such disorders were so exceedingly rare that specializing in the diagnosis and treatment of these disorders was unwarranted. The discovery of new neural autoantibodies aiding diagnosis, and the rapid validation and optimization of test methodologies, has revealed that these conditions are much more common than previously appreciated, and account for many undiagnosed/misdiagnosed patients who require specialty expertise for management of their complex diseases. Traditional subspecialty training in neuroimmunology may not necessarily expose trainees to a sufficient volume of patients with neuronal antibody disease. Autoimmune neurology programs primarily focus on obtaining the skills to interpret the diagnostic and prognostic significance of complex autoantibody profiles, including test sensitivity, specificity, and false-positive and false-negative rates, as well as the evolving landscape of test availability. Autoimmune neurology fellowship programs must teach trainees the specific risks and monitoring necessary to safely manage the often aggressive immunomodulation or immunosuppression required for treatment, with a focus on monitoring for objective markers of improvement to inform a rational data-driven approach to therapy choice and duration.

Autoimmune neurology as a clinical subspecialty is distinct from neuroimmunology in several ways. Clinical training in autoimmune neurology teaches a sound diagnostic approach to patients with suspected autoimmune neurologic disease, including knowledge of the multisystem diagnostics that can be utilized to obtain objective data to support diagnosis. A rational diagnostic treatment approach is essential for patient safety and efficiency. Knowledge regarding the risks of emerging immunotherapies is an essential component of training, specifically including pretreatment testing and prophylaxis, as well as long-term monitoring for chronic complications.

Neurologists specialized in autoimmune disorders must recognize the clinical phenotypes that suggest autoimmunity, and also have intimate understanding of the testing methodology, assay type, as well as sensitivity and specificity of the assay for each validated

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
neural antibody. This requires knowledge of the availability and limitations of assays offered by commercial laboratories within the United States and internationally, as newly discovered antibodies may initially be available for testing at international sites. Optimal training includes exposure to neural antibody diagnostic testing and discovery. Specialists in autoimmune neurology must be able to accurately differentiate known and unclassified antibody syndromes from other disease mimics. The practice of autoimmune neurology includes autoimmune encephalitis, autoimmune epilepsy, autoimmune movement disorders, and dysautonomias, and encompasses the diagnosis and treatment of neurologic complications of systemic disorders, including neurologic accompaniments of systemic lupus erythematosus and Sjögren syndrome, vasculitis (primary CNS vasculitis as well as neurologic manifestations of systemic vasculitis), and neurosarcoidosis.

Autoimmune and paraneoplastic disease can masquerade as classical neurologic disease within all of the traditional neurologic specialties, including epilepsy, cognitive/behavioral, neuromuscular, and movement disorders. Patients may present initially in the inpatient or outpatient setting depending on symptom type and severity. Autoimmune neurologists must be available and competent to consult in both settings. As many autoimmune neurologic disorders present with systemic symptoms, the specialist must be cognizant of manifestations beyond the nervous system.

### TRAINING OPPORTUNITIES IN AUTOIMMUNE NEUROLOGY

There are no nationally accepted accreditation bodies for fellowships in multiple sclerosis, neuroimmunology, neuroinfectious disease, or autoimmune neurology. To ascertain a comprehensive list of all available existing autoimmune neurology fellowships, we utilized 2 approaches to obtain data: we first sought all readily available data by Google searching the terms “autoimmune neurology fellowship” and “autoimmune neurology” (October 2016). Second, we utilized the American Academy of Neurology (AAN) comprehensive fellowships database to search for additional fellowships and to cross-reference the Google data (October 2016). Both sources revealed 4 dedicated fellowships in autoimmune neurology in the United States. Beyond these 4 dedicated autoimmune neurology fellowships, there are numerous other training programs categorized under neuroimmunology or multiple sclerosis fellowship titles that offer variable amounts of exposure to autoimmune neurology. Information about other neuroimmunology and multiple sclerosis fellowships is available on the fellowship directory of the AAN (aan.com/fellowship). Specific information on the 4 dedicated autoimmune neurology programs...
### Table: Autoimmune neurology fellowship programs available in the United States

<table>
<thead>
<tr>
<th>Institution</th>
<th>Years of training</th>
<th>Training offered</th>
<th>Fellowship position(s)</th>
<th>Open to pediatric neurologists</th>
<th>Exposure to neuronal antibody testing</th>
<th>Is there an inpatient component? If yes, describe extent</th>
<th>Diseases seen and treated</th>
<th>Contact information</th>
<th>Date established</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massachusetts General Hospital and Harvard Medical School</td>
<td>1</td>
<td>Clinical</td>
<td>More than 2</td>
<td>No</td>
<td>No</td>
<td>Inpatient consult rotations for autoimmune and infectious cases</td>
<td>NMDARE, LGI-1, other limbic encephalitis, opsonodin myoclonus ataxia syndrome, paraneoplastic neurologic disease, neurosarcoaid, NMO, inflammatory myelopathy, neurologic complications of CTD, CNS vasculitis, neuro-HIV, neurocytomegaly, HSVE, viral encephalitis, neurosyphilis, neuro-Lyme, management of immunotherapy</td>
<td>neuroeducation.massgeneral.org/neurology/fellows/fellowships/advancedgeneralneurology.html</td>
<td>2015</td>
</tr>
<tr>
<td>Mayo Clinic, Rochester, Minnesota</td>
<td>1 or 2</td>
<td>Clinical and research</td>
<td>2 or 3</td>
<td>Yes</td>
<td>Yes, the laboratory receives 150,000 specimens per year; interpretation of tissue IFA, Western blot, and cell-based assays</td>
<td>Yes, consult service</td>
<td>Idiopathic and paraneoplastic autoimmune disorders with and without recognized neural autoantibodies, including encephalopathies, epilepsy, peripheral nerve hyperexcitability (with or without central and autonomic manifestations), movement disorders, cerebellar ataxias, myasthenic syndromes, and gastrointestinal dysmotility; special focus on CNS demyelinating disorders (AQP4, MOG) with option of MS clinic rotation; opportunities for clinical (serologic correlations, epidemiologic studies, therapeutic trials) and bench and translational research (new autoantigen identification, pathophysiology)</td>
<td>mayo.edu/msgme/residencies-fellowships/neurology/autoimmune-neurology-fellowship-minnesota</td>
<td>2005</td>
</tr>
<tr>
<td>University of Utah</td>
<td>1 or 2</td>
<td>Clinical and research</td>
<td>1</td>
<td>Yes</td>
<td>Yes, fellows spend an entire month, full time without other duties, at ARUP Laboratories, devoted to learning neuronal antibody testing, and can be further customized to individual interests; ARUP is located on the campus of the University of Utah</td>
<td>Yes, typically consult on 1-3 inpatients per week, on both pediatric and adult patients</td>
<td>Neuronal antibody-mediated disease, neurosarcoaidosis, neurologic autoimmunity in the context of immunodeficiency or postinfectious syndromes, CNS complications of systemic disease (including Sjögren syndrome, systemic lupus erythematous, and other rheumatologic conditions); patients with MS comprise approximately 5%-10% of the practice</td>
<td>medicine.utah.edu/neurology/neuroimmunology/fellowship/autoimmune-fellowship.php</td>
<td>2013</td>
</tr>
<tr>
<td>University of Texas Southwestern Medical Center</td>
<td>2 or 3</td>
<td>Clinical and research</td>
<td>1</td>
<td>Yes</td>
<td>Yes, limited volume</td>
<td>Yes, consult service</td>
<td>MS, TM, NMO, ADEM, autoimmune encephalitis, autoimmune neuromuscular disorders (including myasthenia gravis, neuromyotonia, and paraneoplastic neuropathies)</td>
<td>utsouthwestern.edu/education/medical-school/departments/neurology/education-and-training/fellowship-programs/autoimmune-disorders.html</td>
<td>2015</td>
</tr>
</tbody>
</table>

**Abbreviations:**
- ADEM - acute disseminated encephalomyelitis
- AQP4 - aquaporin-4 water channel
- CTD - connective tissue disease
- HSVE - herpes simplex virus encephalitis
- IFA - immunofluorescence assay
- LGI-1 - leucine-rich glioma inactivated 1
- MOG - myelin oligodendrocyte glycoprotein
- MS - multiple sclerosis
- NMDARE - NMDA receptor encephalitis
- NMO - neuromyelitis optica
- TM - transverse myelitis
Neurologists trained in autoimmune neurology are a valuable asset to any neurologic practice, because their expertise enables diagnosis of the growing spectrum of autoimmune neurologic conditions, as well as management of immunotherapy and complications of the disorders and their therapies. This skill set is especially relevant because autoimmune disorders intersect all neurologic subspecialties and few neurologists are comfortable prescribing and managing the emerging arsenal of immunotherapy utilized in treating these conditions. A neurologist trained in autoimmune neurology fellowship is likely to practice in an academic institution or a large neuroimmunology clinic where opportunities for basic science and clinical research are available. Combined training with a complementary neurologic subspecialty provides additional practice options because trainees acquire skill to diagnose and treat disorders with an autoimmune etiology that manifests neurologically as a classical specialty syndrome, such as a behavioral/cognitive disorder with unusually rapid progression, or intractable seizure disorder.

Encephalitis is a major public health concern in the United States; over 20,000 patients are hospitalized every year, and in up to 49% of cases, the underlying etiology is undetermined. Recent data show that autoimmune encephalitis is not an uncommon disorder, and in some populations it is more frequent than viral and other causes of encephalitis. The incidence of other autoimmune disorders is unknown but studies show that autoantibodies are found in up to 11% of patients with epilepsy. As the awareness of autoimmune epilepsy continues to increase, it is likely that more patients will be diagnosed and treated appropriately with immunotherapy.

Established experts in autoimmune neurology both in the United States and internationally frequently provide informal consultative assistance to colleagues around the world, underscoring the value of telehealth and cyberconsults, a need that will continue to grow as recognition of autoimmune neurologic disorders outpaces the number of physicians trained in this emerging subspecialty.

With increasing awareness of autoimmune neurologic disorders, academic institutions will no doubt recruit staff neurologists with specific training in autoimmune neurology, and create fellowships with a focus on autoimmune neurology, ideally with formal exposure to neural autoantibody testing. Educating our colleagues from non-neurologic specialties is a major need; as the awareness of autoimmune neurologic disorders continues to increase, creating workshops/lectures dedicated to health care professionals is crucial. Prospective trials are needed in autoimmune neurology in an effort to create evidence-based guidelines for the use of immunotherapy that can help select specific agents and duration. Autoantibody testing in neurology is becoming more frequent as the awareness of immune- and antibody-mediated disorders increases, but ultimately a thorough evaluation of the clinical history and presentation is the most crucial component of the evaluation in these patients, particularly in antibody variants of unknown significance, in order to avoid the possible harm of unnecessary immunotherapy.

ROLE OF AUTOIMMUNE NEUROLOGY IN THE DIAGNOSIS OF CANCER

Neurologic autoimmunity is often triggered by an underlying systemic neoplasm. Recognition of an informative profile of autoantibodies in serum and spinal fluid focuses the oncologic evaluation and guides appropriate therapy, thus improving the outcome significantly. Treatment of underlying malignancy does not always ameliorate the associated neurologic syndrome. A close working relationship among the autoimmune neurologist, neuro-oncologist, and oncologist is ideal for optimal patient management.

Paraneoplastic neurologic syndromes are rare and affect 1/10,000 patients with cancer; however, as the life expectancy continues to increase, the incidence of cancer and thus the incidence of paraneoplastic syndromes is also expected to increase, creating a need for expertise in diagnosis and treatment of these disorders. The frequency of underlying tumor is different depending on the autoantibody type, and the creation of guidelines for screening is of major importance to avoid unnecessary radiation exposure or excessive anxiety in patients.

CONCLUSION

Autoimmune neurology is a rapidly developing subspecialty driven by continuing autoantibody discoveries and increasing recognition of autoimmunity as the basis of neurologic conditions previously misdiagnosed, for example, as degenerative, vascular, or infectious. Gaining expertise in the diagnosis and acute and chronic management of these complex conditions should be an integral component of contemporary neurology practice.

AUTHOR CONTRIBUTIONS

Dr. Lopez contributed to the conception and design of the study; collection, analysis, and interpretation of the data; drafting and critical revision of the article; and generation/collection of the figures. Dr. Clardy contributed to the conception and design of the study; collection, analysis, and interpretation of the data; drafting and critical revision of the article; and generation/collection of the figures. All authors gave final approval of the article.

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DISCLOSURE
A. López-Chiriboga is the incoming autoimmune neurology fellow at Mayo Clinic (2017–2018). S. Clardy is the Director of the autoimmune neurology clinic at the University of Utah and a graduate of the autoimmune neurology fellowship at Mayo Clinic. Go to Neurology.org for full disclosures.

EDITOR’S NOTE
The goal of the Emerging Subspecialties subsection of the Neurology Resident & Fellow Section is to educate neurology residents regarding the history and development of new subspecialties. The articles are first-authored by residents and provide the unique perspective of a trainee interested in the topic and faced with various fellowship opportunities and career pathways. This article is the opinion of the authors and has not been endorsed by the new AAN Section of Autoimmune Neurology.

REFERENCES

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International Issues

More than 85% of the world's population lives in low and middle income countries, where the burden of neurologic disease is greatest. In addition, over 50 million Americans live in medically underserved communities. Despite these figures, relatively little is known about patients and practitioners of neurology in resource-limited settings. This section aims to explore global and community health topics in neurology education. We welcome manuscripts describing international educational exchanges, personal rotations in low and middle income countries, and work by neurology trainees from around the world. We also welcome manuscripts that discuss community health initiatives and volunteer experiences in underserved regions of the United States. Inclusion of practical information on local or international volunteer opportunities would also be of use.
International Issues: Teleneurology in humanitarian crises
Lessons from the Médecins Sans Frontières experience

ABSTRACT
Humanitarian emergencies defined by armed conflict, political strife, famine, or natural disaster can devastate populations rapidly. Neurologic disorders accompany these complex humanitarian emergencies but often go unheeded, exacerbated by a scarcity of neurologists. Teleneurology offers the promise of neurologic care remotely in the face of this inadequate local clinician supply. We describe our experiences as voluntary neurology teleconsultants with Médecins Sans Frontières in order to highlight both the promises and challenges of teleneurology in humanitarian contexts. We identified the major advantages of this service as (1) minimal resources and incurred costs while (2) changing a patient’s clinical course favorably, and (3) creating a community for the field referrer and neurology specialist. Current challenges include (1) limited diagnostic resources and difficult diagnostic and therapeutic decision-making, (2) need for greater continuity and familiarity between the field site and neurologist, (3) gaps in the US neurology curriculum to provide expertise for all sites, (4) lack of follow-up and feedback from the field to advise future cases, and (5) low frequency of consultations. Growth opportunities include eventual expansion to the development of a community of neurologists who can provide context-specific care and maximize use of multimedia at low Internet bandwidth. Lessons from our experience may help optimize teleneurology’s effect and reduce disparities in neurologic care, particularly in humanitarian crises. Neurology® 2017;89:e16–e19

GLOSSARY
AED = antiepileptic drug; MSF = Médecins Sans Frontières; TBI = traumatic brain injury.

Humanitarian crises present distinct challenges for the provision of neurologic care, but provide opportunities to implement innovative technologies across traditional boundaries. In settings of armed conflict, famine, political strife, natural disaster, or a combination of these devastating situations, neurologists are generally absent.1 In some cases, there were never neurologists in these locations: in low-income countries in general, there is an estimated average of 3 neurologists per 10 million people, compared to high-income countries, where the same number exists for 100,000 people, a 100-fold difference.2 In sub-Saharan African in particular, there is an estimated 0.6 neurologists per million people.3 In other situations, health care workers flee in times of emergency or are targeted.4 Meanwhile, the number of people who can access mobile devices and some form of Internet is increasing rapidly, especially in new locations across Asia, Africa, and the Middle East.5 Innovative solutions are almost certainly needed to facilitate access for neurologists in humanitarian emergencies, using newer technologies that have the potential to improve the lives of patients with neurologic disorders.

Over the last 2 years, we have voluntarily provided teleneurology consultations with Médecins Sans Frontières (MSF), a medical humanitarian emergency nonprofit organization that has 450 projects in 69 countries in addition to their search and rescue operations.5 From this experience, we have been able to identify some potential pitfalls and challenges in developing and using teleneurology in the context of humanitarian crises. Teleneurology can serve a meaningful role in the provision of neurologic care in the face of a limited clinician supply, and we hope lessons from our experience will be valuable for future efforts by organizations engaged with public health and neurology.

THE PROMISE OF TELEMEDICINE/TELENEUROLOGY

Telemedicine is a burgeoning technology that allows the exchange of medical information between health care practitioners from...
disparate geographic areas to assist in patient diagnosis and treatment. The American telemedicine market is projected to grow 20%–50% annually, reaching a $30 billion USD industry by 2019.6 Currently, telemedicine services are used by nearly 50% of acute care hospitals.7,8

Telemedicine can take on many forms. For example, teleconsultations can occur in a synchronous or asynchronous manner. Synchronous telemedicine enables real-time communication. Asynchronous telemedicine features delayed communication, with data transmitted electronically and reviewed by patients or health care practitioners at a later time. This is also known as a store-and-forward system of telehealth consultation.

Teleneurology is a branch of telemedicine that allows consults and practices through remote neurologic evaluation, and has seen similar growth.9 It is often touted as a potential solution to the growing demand for neurologic services that outmatches the supply of neurologists,10 a demand which exists both domestically and globally.

BRIEF OVERVIEW OF MSF SYSTEM AND CASES In 2010, MSF launched a telemedicine project using store-and-forward methods based on the Collegium Telemedicus platform.11 This web-based messaging system provides doctors at its field sites with access to a wide range of specialists, including neurologists. Specialists provide purely advisory consultations, with the final patient management decisions remaining with physicians in the field. Correspondences are stored securely on the telemedicine server for ease of future reference. To date, more than 150 consults have been provided by >10 neurologists living in 6 countries. Physicians in the telemedicine consultant service must have an active medical license and are recruited through professional connections and recognized experience in field settings overseas. The neurology consultants collectively speak English, French, and Spanish, and there are translation services available if the referrer’s questions are in an alternative language. The consultant group includes 3 pediatric neurologists.

PROMISES AND OPPORTUNITIES The potential benefits of teleneurology in humanitarian crises involve the provider on the ground, the neurologist remotely, and the patient.

Minimal resources and costs incurred. The infrastructure required for both the clinical referrer and neurologist to access this service is minimal—a computer and Internet access. There are no extra computer programs or software since the telemedicine system is accessed through a web browser. Given the store-and-forward approach, a constant Internet connection is not even required. Internet connection can be established for a temporary period of time in order to access and relay the necessary information. The dramatic growth of global mobile subscriptions, including in low-income households across Africa and Asia, promises to expand telemedicine’s reach.5 Providing neurologic care via telemedicine systems in humanitarian emergencies therefore may not need to be sophisticated to deliver benefit. There is also a substantial cost reduction associated with avoiding expensive referrals in regions where there is a chronic shortage of specialists.12 In this case, the neurologists are volunteering their time, making the service free.

Changing the patient’s clinical course. In several cases, we were able to provide assistance in changing the diagnosis or management of patients. For example, one with traumatic brain injury (TBI) and post-TBI seizures was recommended to have an extended duration of an antiepileptic drug (AED) and lifelong therapy if seizures recur with AED dose reduction.13 In a second patient, we added acyclovir and antibiotic coverage for methicillin-resistant Staphylococcus aureus to the antibiotic regimen of a persistently febrile child with seizures. In a 2013 article presenting perspectives of referrers and specialists using the MSF system, 91% of referrers found the consultations to be beneficial, stating that the consult clarified their diagnosis, assisted with management of the patient, and was educationally valuable.14 For physicians in the field who are working in highly stressful circumstances, an additional clinical sounding board can be critical.

Creating a community for referrer and specialist. The interest in global and humanitarian neurology is increasing among neurologists,15 and teleneurology offers an additional opportunity for the burgeoning field of global neurology. One of the benefits we have experienced is being able to identify and work with other physicians who share our interest in applying our neurologic expertise to resource-limited settings. Telemedicine has also been shown to help reduce the feeling of isolation of field doctors,16 as well as offering distance education for field health workers who otherwise have few opportunities to enhance their specialty knowledge and training.

PITFALLS AND CHALLENGES While there is great promise for the use of teleneurology in humanitarian contexts, several limitations remain.

Limited diagnostic resources and difficult decision-making. Even basic imaging and laboratory tests are often not available in humanitarian settings, making proposing appropriate recommendations difficult. When imaging is available, transferring this information with limited Internet access can be especially
challenging due to low bandwidth Internet connections, although even in low bandwidth settings, photographs can be uploaded with considerable patience. Empiric treatment can be offered for syndromic presentations, but can pose potential adverse effects or toxicities, or create a cost burden. Generally speaking, there is a shift from the traditional approach of securing a final neurologic diagnosis—which in our experience occurred rarely—to a focus on neurologic disease categories and sinister and not-to-miss diagnoses and their treatments.

Further, clinicians in the field are not equipped or trained to provide answers even about the neurologic examination without a mastery of neurologic language, examination tools such as a reflex hammer, or confidence in performing a reliable neurologic examination. For the neurologist, this can contribute to a feeling of “shooting in the dark at a moving target.” In a 2015 study of the MSF telemedicine experience assessing user feedback, 33% of specialists stated that the information supplied by the referrer was inadequate.17

**Familiarity between the field site and the neurologist.** The neurologist’s understanding of individual site resources and local disease epidemiology is critical in informing appropriate clinical recommendations. For example, one patient’s case was informed by an understanding of a measles outbreak in Democratic Republic of Congo. Further, Konzo—an irreversible, static, and symmetric myeloneuropathy associated with high dietary cyanogen intake from inadequately processed bitter cassava roots—can only be considered if the consultant is aware of whether cassava is part of the African diet where the case question originates. As cases from the same field site became more frequent, we found that our consultations also became more targeted as our awareness of the local disease burden and available resources increased. The telemedicine platform itself does not provide surveillance, epidemic, or epidemiologic resources to consultants. Therefore, they must be aware of available resources on outbreaks, regional disease risk, and vaccination and dietary patterns.

**Gaps in US-based neurology education.** The cases we saw included a substantial number of pediatric cases, tropical and other infectious diseases including vaccine-preventable diseases, and traumatic cases. These areas are often not well integrated in US curricula for neurology residents and fellows, or represent topical areas where residents and fellows have more limited clinical exposure. One of the authors (F.J.M.) obtained fellowship training in neuroimmunology and neurologic infectious diseases, as well as completing fieldwork in resource-limited settings abroad through a PhD in International Health, consultancies with the WHO, United Nations High Commissioner for Refugees, Polio Eradication Initiative, and refugee-centered nongovernmental organizations, focused in Africa, the Middle East, and Asia. The other author (A.S.) completed several international electives including in sub-Saharan Africa to bolster her knowledge of neurologic care in resource-limited settings. The MSF service itself provides no updated epidemic information data or outbreak or regional information. The authors are aware of and could thus readily access data via the Polio Eradication Initiative (polioeradication.org), Eurosurveillance (eurosurveillance.org), and the CDC Yellowbook (cdc.gov/features/yellowbook/), among other relevant resources. US-based neurologists without an interest or experience in neurologic care in low- and middle-income countries may therefore be suboptimally positioned to provide meaningful advice.

**Infrequent follow-up and feedback from the field.** We found one of the limitations to the experience was absence of consistent patient follow-up information, which made it difficult to assess the outcome of our consultations. We received follow-up about a patient’s progress in 30% of cases. In the cases for which we received feedback from the field physician (e.g., about the feasibility of our recommendations), we were able to improve our recommendations for future consultations, but this practice was not routine. In a survey of referrers and specialists using the MSF telemedicine platform, 45% stated that they had provided feedback about the patient to the specialist; however, 92% of the specialists reported not receiving any feedback about the patient.14 The MSF field environment, with rapid turnover of staff and patients often not returning after discharge, likely contributes to this lower referrer feedback.

**Low frequency of consultations.** In a period of approximately 1 year, we received only 10 consultations. We are among >10 neurologists listed in the MSF database, with 150 cases managed among the group. However, we suspect that the prevalence of people with neurologic diseases exceeds the 150 cases for which there were teleneurology consultations. In a retrospective analysis of neurologic diseases seen in 127 refugee camps monitored by the United Nations High Commissioner for Refugees, visits for sentinel neurologic diseases were in the range of thousands.18 Low uptake of the telemedicine service could be due to several reasons, including low promotion of the service at field sites, limited time, potential language barrier of the referring physician, or resource constraints at field sites preventing use of telemedicine services. With regards to neurologic questions in particular, we anticipate that most likely potential factors are a lack of recognition of neurologic issues or belief that limited resources affect what can actually be
offered in the field. The staccato nature of consults—although seemingly positive on one hand, due to the low time commitment required on the neurologists' behalf—can also be difficult in that timely replies (typically within 24 hours) are required.

**DISCUSSION** Telemedicine can create access to, and reduce the cost of, specialty neurologic care by facilitating the provision of expertise at remote sites, particularly in resource-limited humanitarian settings, where there is a disproportionate burden of neurologic disease. Neurologists may be uncertain about the value they add in a humanitarian crisis, but our experience tells us we are at times critically needed and can make a significant impact. Of course, introducing any novel technology in health care comes with inevitable challenges, but an iterative process involving user feedback can lend itself to making the technology more affordable, available, and timely. The MSF experience highlights the need for improved resource availability for neurologic disorders in resource-limited settings, increasing familiarity of neurologists with the background of the country they represent and the importance of follow-up and feedback as potential areas of growth for future teleneurology projects in humanitarian crises.

**AUTHOR CONTRIBUTIONS**

Dr. Saadi: design or conceptualization of study, analysis and interpretation of data, drafting or revising the manuscript. Dr. Mateen: design or conceptualization of study, study supervision, critical revision of manuscript for intellectual content.

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**DISCLOSURE**

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**REFERENCES**


Neurology Journal Club

Neurology® Journal Club submissions are structured evaluations of recent Neurology research articles. The aim is to enhance the training of residents and fellows by instruction in the critical appraisal of medical literature. Residents or fellows interested in submitting a Neurology Journal Club article should review the e-Publication Ahead of Print articles at NPub.org/aheadofprint for the most recently published material and email Neurology with their selection for prior approval. Selections will aim to represent the major categories of research methodology over the course of a three-year residency cycle. Submissions should be timely and are requested no longer than four weeks following the original e-publication date of the subject article. These Journal Club critiques, written by neurology residents and fellows with faculty supervision, should follow a specific outline and contain subtitles for background and significance, hypothesis and design, methods, results, and interpretation. Rather than a critical correspondence or editorial, this feature will highlight methods for the critical appraisal of medical literature. This online feature could be used as an adjunct to traditional institutional journal clubs and promote discussion among neurologists, including trainees and those in practice.
Journal Club:
Long-term functional outcome in patients with acquired infections after acute spinal cord injury

Infections, particularly pneumonia, are the primary cause of mortality in individuals with spinal cord injury (SCI).\(^1\) Several factors may contribute to the high rate of infections in the SCI population, including motor paralysis and reduced reflexes resulting in aspiration, invasive procedures, and so-called SCI-induced immune depression syndrome (SCI-IDS).\(^2,3\)

SCI-IDS is thought to occur when the connection between the CNS and the immune system are disrupted by a lesion in the spinal cord, resulting in a decrease in immune function.\(^3\) In addition to increased morbidity and mortality, infections after SCI may affect neurologic recovery.\(^2,3\) A recent study found that infections impaired the return of muscle strength up to 1 year postinjury; however, the long-term consequences remain uncertain.\(^2\)

The aim of this study was to investigate whether infections occurring in an acute care setting after SCI affected long-term functional recovery and survival.\(^4\)

**METHODS** Data source and inclusion criteria. The study by Kopp et al.\(^4\) used data gathered from the multicenter National Spinal Cord Injury Database (NSCID). The NSCID prospectively gathers data from 25 specialized traumatic SCI care centers.\(^2\)

Inclusion criteria were admission within 24 hours after injury between 1995 and 2005, age between 17 and 75, a cervical SCI, complete baseline and infection data, and an American Spinal Cord Injury Association Impairment Scale (AIS) grade of A, B, or C (see table e-1 at Neurology.org for a full description of the AIS grading system). Participants were excluded if they resided in a hospital or nursing home prior to injury, had serious concomitant injuries affecting consciousness, or were rehospitalized for unspecified infectious or parasitic diseases during the follow-up period.

**Exposures and outcomes.** The primary outcomes were the FIM motor scores as a dependent variable and an additional model (adjusted for AIS, level of injury, age, ethnic group, and working status), and finally 3 models stratified for AIS grade and adjusted for the aforementioned variables.

Mortality data were analyzed using an exploratory analysis and a Cox regression model (adjusted and unadjusted) over 10 years. Similar to the LMM, the Cox models were adjusted for AIS, stratified for AIS, and further adjusted for neurologic level of injury, age, working status, and educational level.

**RESULTS** A total of 1,203 individuals were included in the study, with 47% (564) acquiring an infection during early care, the majority of which were pneumonia (540 acquired pneumonia, 11 postoperative wound infections, and 13 both). The group that acquired infections was significantly different from the group that did not with regards to sex (a higher proportion of males), injury severity (a higher proportion of AIS As), level of injury (a higher proportion of C1–C4 injuries), and median baseline FIM\(_{motor}\) scores (a smaller interquartile range).

The exploratory analysis in the complete cohort and the AIS A group identified significantly higher FIM\(_{motor}\) scores in those without acute infections at each time point. The AIS B and C group analyses only found a significant difference between the 2 groups at discharge.


Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
The FIMmotor score LMMs not stratified by AIS (imputed and complete cases models) all revealed a significant association between acquired infections and impaired recovery of FIMmotor scores at each time point, and overall. Specifically, the imputed model adjusted for all variables revealed a $-7.4$ point difference (95% confidence interval [CI] $-11.5$ to $-3.3$) and the complete cases model revealed a $-5.2$ point difference (95% CI $-8.4$ to $-2.0$). The model was then stratified by AIS and adjusted for level of injury and sociodemographic variables. When the model was stratified by AIS grade, there was an overall significant association between infections and impaired recovery in AIS A (both models) and in AIS B at 5 years for the imputed model only. The AIS C model did not confer an overall significant association.

In-hospital mortality was not significantly different between the groups with and without infections; however, Kaplan-Meier survival curves indicated a significant difference in survival in both the total cohort and AIS subgroups over a 10-year period. Initial Cox regression confirmed a significant association between infection and mortality in the total cohort with and without adjustment for AIS grade, and stratification by AIS grade revealed an association in AIS A and B. Further adjustment for level of injury and sociodemographic variables (age, working status, and educational level) confirmed the significant association in the complete cohort (hazard ratio 1.65, 95% CI 1.26–2.16) and the AIS A stratification.

**INTERPRETATION** This work indicates that pneumonia and postoperative infections in acute care after SCI negatively affect both long-term functional recovery and survival. This study was conducted using an observational database. Although this design introduces the possibility of additional factors related to the exposure (infections) influencing the outcomes, the study design is suitable for the nature of the study as it is not possible to randomize individuals to the study exposure.

The authors provide a strong statistical analysis investigating the association between early infections after SCI and long-term functional recovery and mortality utilizing multiple imputation to account for attrition bias. Attrition, or loss to follow-up, can occur for numerous reasons, and is of particular concern in longitudinal studies. These missing data can introduce bias when the lack of data is related to the outcome measure, and is not missing at random. One strategy to avoid this bias is multiple imputation, in which missing values are predicted through other observed values in the dataset, creating multiple imputed datasets, and averaging these imputed estimates. This is a common method of accounting for missing data, with varying outcomes. Presented in conjunction with the complete case sensitivity analysis, the imputed data allow for a transparent interpretation of the results. In addition, the authors also adjust for variables known to be related to functional recovery after SCI (e.g., level of injury, AIS). The results consistently confirm that early infections are associated with impaired functional outcomes after SCI in complete SCI. The authors note that these effects are likely due to pneumonia, as this accounted for the majority of recorded infections.

Based on stratified sensitivity analyses, the authors reported that attrition bias existed in AIS groups B and C, but not A, due to the fact that the imputed and complete case only models produced differing results. This could indeed be due to attrition bias, or inaccuracy in the imputations. It would be of interest to examine whether this was due to a nonrandom dropout in the groups AIS B and C, and not A.

Given that the cohort included patients enrolled between 1995 and 2005, it would be of interest to know how the management of care after SCI (e.g., infections and treatments for infections) changed throughout this time frame, or if year of admission differed significantly between the groups. Perhaps related to care, length of acute care stay has also been shown to affect functional outcomes after SCI, and could provide further insight.

Regarding inclusion/exclusion criteria, the authors provided valid reasoning for the inclusion of specific injury characteristics (limiting heterogeneity and ceiling effects in recovery), though no reason was given for the exclusion of individuals in prior care. Second, patients who were rehospitalized for unspecified infectious or parasitic diseases during follow-up were also excluded, and a justification was also not provided. Both prior care and rehospitalization could potentially confound the relationship between infection and function/survival, which may have been the reason for their exclusion. However, it would be interesting to quantify how these factors affected the study outcomes in a sensitivity analysis. Third, of all the individuals who were enrolled in NSCID and met the initial selection criteria (n = 1,427), 1,203 (84%) remained after the application of the exclusion criteria. Exclusion was largely due to age and missing baseline assessments. Although the proportion of patients recruited was high, it would be of interest to know if those excluded due to missing data differed significantly with regards to injury characteristics or outcomes.

Overall, this article provides a strong statistical analysis of the available data and presents a comprehensive report of the outcomes. Future analyses on novel cohorts and potential confounding and mediating variables could increase our understanding of how
acute infections after SCI are related to long-term functional recovery.

AUTHOR CONTRIBUTIONS
F.M. Warner: drafting/revising the manuscript, analysis or interpretation of data. B. Tong: revising the manuscript, analysis or interpretation of data. Dr. Jutzeler: revising the manuscript, analysis or interpretation of data. Dr. Cragg: revising the manuscript, analysis or interpretation of data. P.S. Scheuren: revising the manuscript. Dr. Kramer: drafting/revising the manuscript, analysis or interpretation of data.

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The authors declare no competing financial interests. Go to Neurology.org for full disclosures.

REFERENCES

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AAN members are urged to submit medically or scientifically related artistic images, such as photographs, photomicrographs, and paintings, to the "Visions" section of Neurology®. These images are creative in nature, rather than the medically instructive images published in the NeuroImages section. The image or series of up to six images may be black and white or color and must fit into one published journal page. Accompanying description should be 100 words or less; the title should be a maximum of 96 characters including spaces and punctuation.

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Mystery Case

Interesting teaching cases submitted to the Resident & Fellow Section are chosen by the editors to be published under the new Mystery Case subcategory. The Neurology® editorial office disseminates a teaser through social media before the case is published. This usually includes a short description of the case, video or partial figure, and one to three questions. Responses are compiled and then published with the full case.
Mystery Case:
Acute hydrocephalus caused by radiographically occult fourth ventricular outlet obstruction

A 19-year-old woman with no history of CNS inflammatory pathology or hemorrhage presented with 5 days of diplopia and headache. Examination revealed papilledema and bilateral sixth nerve palsies. Imaging demonstrated panventricular enlargement and marked 4th ventricular dilation (figure 1). Cine MRI revealed turbulent fourth ventricle CSF flow suggesting outflow obstruction, which was confirmed with contrast ventriculography. A suboccipital craniotomy was then performed, which revealed an arachnoid web (figure 2). Membranous occlusion of the fourth ventricular outlet is a rare cause of obstructive hydrocephalus usually associated with a history of inflammatory conditions or hemorrhage.1 A small number of idiopathic cases have been reported.2

In this case, microsurgical fenestration reconstituted CSF flow and resolved the patient’s diplopia. However, she subsequently required ventriculoperitoneal shunting to resolve recrudescence of persistent headache, indicating both obstructive and communicating components to her hydrocephalus syndrome.

AUTHOR CONTRIBUTIONS
Daniel Duran: construction of figures and text. Muhamed Hadzipasic: construction of figures and text. Kristopher T. Kahle: concept and design, performed suboccipital craniotomy, microsurgical fenestration procedure, acquired photographic images, critical revision of text and figures.

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REFERENCES

MYSTERY CASE RESPONSES
The Mystery Case series was initiated by the Neurology® Resident & Fellow Section to develop the clinical reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses were solicited through a group e-mail sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media. We received 177 responses. The vast majority of respondents (73%) had been in practice for 1–4 years; 53% were residents/fellows while 32% were faculty/

*These authors contributed equally to this work.
From the Departments of Neurosurgery (D.D., K.T.K.), Pediatrics (K.T.K.), and Cellular and Molecular Physiology (K.T.K.), Yale School of Medicine (M.H.), New Haven, CT.
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Neurologists must provide excellent care to an increasingly diverse patient population. According to census projections, the United States will become a majority–minority nation by 2060, with no single ethnic or racial group making up a majority of the population.\(^1\) Diversity of gender, sex, sexual orientation, race, ethnicity, socioeconomic status, age, ability, and religion must be acknowledged and understood in order to provide equitable patient care.

Patients with neurologic disorders experience racial, socioeconomic, and geographic disparities in care and outcomes.\(^2,3\) Furthermore, women and several racial and ethnic groups remain underrepresented in academic neurology (figure).\(^4,5\) and experience inequity in compensation and professional advancement across academic medicine.\(^6,7\)

Academic medicine is uniquely positioned to improve the understanding and promotion of equity, diversity, and inclusion (EDI).\(^8\) Neurology residency training provides a valuable opportunity to educate and engage future neurologists to understand and promote EDI. To our knowledge, there are no structured opportunities for neurology trainees to study these topics.

We created a certificate program focused on EDI within the Harvard Medical School, Brigham and Women’s Hospital, and Massachusetts General Hospital Partners Neurology Residency Program. Prior to 2016, certificate programs existed within the residency program to provide training and mentorship for residents interested in basic science or clinical research, quality improvement, global health, and medical education, but not EDI. By explicitly structuring opportunities for trainees to validate and encourage EDI scholarship, rather than passively acknowledging diversity within the residency, we aimed to more fully realize the goal of advancing EDI.

**CREATING A DIVERSITY AND INCLUSION CERTIFICATE PROGRAM** Kern\(^9\) proposed an approach to curriculum development for medical trainees, including residents. The 6 steps are (1) problem identification, (2) assessing the needs of the specific learners to be targeted, (3) determining goals and objectives, (4) choosing an educational strategy, (5) implementation, and (6) evaluation and feedback. Although the initial idea for the certificate program arose informally during discussions among residents and faculty members, all 6 steps were ultimately addressed over the course of the program’s creation.

First, residents and faculty identified the problem: gaps in diversity among trainees that included were not limited to gender and racial diversity, along with often unconscious barriers to inclusion and success for all trainees. Residents, the specific learners to be targeted by the program, identified a need for more formal training in the study and promotion of EDI, both within residency training and within academic neurology. Our goal was to offer a structured educational opportunity that would allow interested residents to connect with mentors and develop the skills necessary to advocate for EDI within their current training environment and over the course of their careers. This structured mentorship and training framework considered the reality of academic medicine’s reliance on sponsorship and patronage in all areas, including EDI.

Certificate programs in research, quality improvement, global health, and medical education have been well-received within the residency program since 2014 and thus we chose a certificate program as the educational strategy for this initiative. As with the existing certificate programs, proposed requirements included choosing a mentor, joining a relevant institutional or departmental committee, designing a scholarly project, submitting an abstract or manuscript for presentation or publication, and presenting the results to peers and faculty.

The certificate program was launched in the spring of 2016. Evaluation and feedback mechanisms for the existing certificate programs, including online evaluations and semiannual meetings, will be used to track future outcomes.

**PRELIMINARY OUTCOMES OF THE CERTIFICATE PROGRAM** As of October 2016, 4/34 (11.8%) of eligible PGY-3 and PGY-4 residents enrolled in the new program.
Certificate program. This is comparable to the number of residents enrolled in the first year of other certificate programs (research = 3; medical education = 4; quality and safety = 4; global and humanitarian health = 2), and is expected to similarly increase.

**CASE STUDIES**

**Case study 1.** One of the certificate program participants (A.S.) was mentored by one of the coauthors (N.I.M.). With other collaborators, they wrote an article about disparities in neurologic health care access among black, Hispanic, uninsured, and low-income patients, which was published in *Neurology* and presented at the 2017 American Academy of Neurology annual meeting. Within the residency, the participant organized a monthly lecture series on EDI issues, including lectures on unconscious bias, caring for the Boston homeless population and patients with limited English proficiency, and physician advocacy. The resident also served on the Massachusetts General Hospital (MGH) Neurology Diversity Committee, which meets monthly to discuss community and department-based diversity-related initiatives, and attended sessions organized by the MGH Center for Diversity and Inclusion.

**Case study 2.** Another certificate program participant (A.M.B.) was mentored by a physical medicine and rehabilitation physician who directs a Harvard Medical School Continuing Medical Education course titled “Career Advancement and Leadership for Women in Healthcare.” The resident attended the course, assisted with organizational tasks, and networked with the course speakers. Together with an interdisciplinary team of coauthors, she and her mentor published an article in the journal *PM&R* about the role of gender in academic medicine. In conjunction with the residency program directors and chief residents, she also worked to increase the visibility of female faculty members during residency applicant interview days, both during didactic lectures and through individual meetings with applicants. Along with 2 of the coauthors (K.E.M., J.L.L.), she secured funding from the residency and the American Academy of Neurology (AAN) to send 11 residents to the AAN’s Women’s Leadership course at the 2016 Breakthroughs in Neurology Conference.

As these case studies demonstrate, residents and mentors alike have benefited from this program. In the words of a resident participant:

> This program is important to me because not only does its mere existence acknowledge that there are many issues with diversity and inclusion among our hospitals, but also it provides a platform to address these issues.
According to one of the mentors:

Developing and launching the program gave me an opportunity to partner with trainees. Together, we developed an idea that seemed meaningful to both faculty and residents. The new format has formalized relationships and brought greater accountability with regards to the outcomes of our collaborations. In a short time, fruitful projects have emerged and led to new programs, research presentations, and publications.

**IMPLICATIONS AND FUTURE DIRECTIONS** The creation of an EDI program for neurology trainees is feasible. Initial enrollment and outcomes suggest that the program responds to neurology trainee needs and interests. Immediate results of this educational initiative have already led to positive changes. An added benefit of this program is its contribution to meeting Accreditation Council for Graduate Medical Education Program Requirements for Graduate Medical Education in Neurology that advocate for “sensitivity and responsiveness to a diverse patient population” and “an awareness of and responsiveness to the larger context and system of health care.”

Scholarly activity promoting EDI as an essential part of academic neurology can nurture a skilled, impassioned, and increasingly diverse workforce committed to eliminating disparities affecting patients and physicians. We encourage implementation of similar initiatives in neurology training programs throughout the country.

**AUTHOR CONTRIBUTIONS**

Anna M. Bank and Altaf Saadi contributed equally to design, conception, and drafting of this manuscript and critical revision of the article. Kathleen E. McKee, Nicte I. Mejia, and Jennifer L. Lyons provided critical revision of the article. All authors approved the final submitted version.

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**REFERENCES**

Pearls & Oy-sters

“Pearls and Oy-sters” is a feature focusing on fundamental clinical neurology. Each article addresses a specific niche of neurological disease and provide expertise in the form of clinical insights and tips, i.e., “pearls,” as well as advice for avoiding mistakes, or “oy-sters.” The author may choose to address a particular facet of the approach to neurological disease such as localization, elaboration of a differential diagnosis, evaluation, or treatment. These articles concentrate on what may be found in a textbook and/or provide what textbooks cannot, in the form of knowledge rendered from clinical experience. The target audience consists of those in training; however, the subject matter should be of interest to all in the world of clinical neurology.
Pearls & Oy-sters: Asymmetric meningeal involvement is a common feature of rheumatoid meningitis

PEARLS

• Rheumatoid meningitis is a rare complication of rheumatoid arthritis that requires a meningeal biopsy for diagnosis.

• Asymmetric meningeal involvement is a common, although not pathognomonic, brain MRI finding in rheumatoid meningitis.

OY-STERs

• Because various immunosuppressants are used for the treatment of rheumatoid arthritis, a thorough investigation to exclude opportunistic infections should be conducted before the diagnosis of rheumatoid meningitis.

• Immunoglobulin G4–related disease, granulomatous diseases such as granulomatosis with polyangiitis, neurosarcoidosis, neurophilis, and meningeal metastasis are possible considerations in the differential diagnosis of rheumatoid meningitis.

CASE REPORT

A 65-year-old woman with a 3-year history of rheumatoid arthritis presented with headache, confusion, a decreased level of consciousness, and recurrent left hemiparesis. Her rheumatoid arthritis was well-controlled with oral prednisolone, methotrexate, and leflunomide. Serum levels of rheumatoid factor and anticyclic citrullinated peptide antibody were 69.3 and 48.8 U/mL, respectively. Brain MRI revealed mild hydrocephalus and diffuse asymmetric high signal intensities with patchy nodules, which were prominent along the leptomeninges and subarachnoid space of the right frontoparietal lobe on fluid-attenuated inversion recovery (FLAIR) images and diffusion-weighted imaging (DWI). Gadolinium uptake was observed in the leptomeninges over the right hemisphere on postcontrast T1-weighted images (figure 1, A–C). The results of CSF analysis showed an opening pressure of 15 cm H2O, leukocyte count of 20/μL (54% neutrophils, 31% lymphocytes, 15% other cells), protein level of 113.4 mg/dL, and glucose level of 43 mg/dL; however, within 2 weeks, the CSF opening pressure became elevated, reaching 27 cm H2O. In addition, CSF rheumatoid factor was detected at a level of 17.6 IU/mL. An extensive workup for infectious diseases, autoimmune diseases including vasculitis, and leptomeningeal metastasis was performed. CSF cytology for malignant cells as well as Gram stain and culture were negative. Tests for Mycobacterium tuberculosis and fungus in the CSF were negative. CSF PCR results for Hemophilus influenzae, Streptococcus agalactiae, Neisseria meningitidis, Streptococcus pneumoniae, Listeria monocytogenes, herpes simplex virus, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, and enterovirus were negative. Serum levels of immunoglobulin G subclass IV (IgG4), antinuclear antibody, anti-neutrophil cytoplasmic antibodies, anti-dsDNA antibody, anti-Ro/La antibodies, and angiotensin converting enzyme were normal. The EEG results showed regional slowing in the right frontocentral region. A biopsy from the right frontal meninges revealed necrotic granulomatous inflammation with dense infiltration of CD68-positive histiocytes as well as focal vasculitis in the leptomeninges (figure 1, D–F). Rheumatoid nodules were not present. In contrast to the leptomeninges, brain parenchyma and the pachymeninges were not involved (figure e-1 at Neurology.org). Acid-fast bacilli stain and culture with a nested PCR for tuberculosis in the biopsy specimen were negative. These findings were consistent with rheumatoid meningitis. The patient’s left hemiparesis had started to improve with the insertion of extraventricular drainage. She was successfully restored to her premorbid functional status with high-dose IV methylprednisolone pulse therapy (1,000 mg daily for 5 days) and subsequent oral prednisolone at 60 mg daily. This patient presented a rare case of rheumatoid meningitis and demonstrated the notable MRI appearance of asymmetric leptomeningeal involvement.
DISCUSSION In this case, the patient developed recurrent left hemiparesis during admission and showed definite asymmetry on brain MRI. Unilateral meningeal involvement in rheumatoid meningitis is not considered uncommon. Some previous cases had presented with stroke-like episodes of abrupt-onset hemiparesis. In contrast, relatively few cases of rheumatoid meningitis show diffuse symmetric meningeal enhancement. Brain MRI findings, which demonstrate unilateral meningeal thickening with high signal intensities along the adjacent subarachnoid space on FLAIR images, and bright signals on DWI are helpful to support diagnosis; however, to our knowledge, the diagnostic importance of asymmetry on brain MRI in rheumatoid meningitis has not been systematically evaluated. To investigate how frequently asymmetry on brain MRI is observed in patients with rheumatoid meningitis, a systematic search of publications listed in PubMed from 2005 to 2016 was conducted using the keywords “rheumatoid” with “meningitis,” “leptomeningitis,” and “pachymeningitis.” In total, 28 case reports in English were collected. We reviewed a total of 29 patients with rheumatoid meningitis including the present case. Among them, about 62% of cases (18/29) showed definite asymmetric meningeal involvement on brain MRI. Furthermore, most patients had developed hemiparesis or hemibody sensory changes mimicking acute stroke or localization-related epilepsy in the course of the disease (table e-1).

The CSF findings commonly observed in rheumatoid meningitis seem to be nonspecific. Most patients showed mild pleocytosis that is predominantly composed of mononuclear cells, a slightly elevated protein level, and a normal or slightly reduced level of glucose, although one case demonstrated 46,000 leukocytes/μL in CSF. Some authors suggested that CSF rheumatoid factor and interleukin-6 could be elevated in patients with rheumatoid meningitis. The present case also demonstrated an elevated level of rheumatoid factor in CSF. However, the diagnostic utility of rheumatoid factor or interleukin-6 in CSF has not been validated. The diagnosis of rheumatoid meningitis still relies on microscopic examination following an invasive meningeal biopsy, despite early diagnosis and prompt immunotherapy being considered important in improving patients’ prognoses. The histopathologic findings suggestive of rheumatoid

Figure 1  Brain MRI and histopathologic findings of the biopsy

(A) Axial fluid-attenuated inversion recovery (FLAIR) image demonstrates diffuse high signal intensities overlying the bilateral leptomeninges and subarachnoid space, which shows asymmetric meningeal involvement, more definite in the right frontoparietal area (white arrows) than in the left side (yellow arrows). (B) Axial diffusion-weighted imaging (DWI) shows diffuse meningeal high signal intensities with patchy nodules, more prominent in the right cerebral hemisphere (white arrows) compared with the left side (yellow arrows). (C) Contrast-enhanced coronal T1-weighted image shows distinct leptomeningeal enhancement over the right frontoparietal lobe (white arrows). (D) Meningeal biopsy reveals chronic granulomatous inflammation with necrotic changes in the leptomeninges (hematoxylin & eosin staining, ×200). (E) Non-necrotizing vasculitis in medium-sized vessel with infiltration of mixed inflammatory cells (hematoxylin & eosin staining, ×400). (F) Immunostaining demonstrates infiltration of CD68-positive histiocytes surrounding granuloma (×200).
meningitis include meningeal inflammation, rheumatoid nodules, and vasculitis. The meningeal infiltrate consists primarily of mononuclear cells including lymphocytes and histiocytes. Notably, the majority of case reports did not show an invasion of brain parenchyma, except for a few cases demonstrating nonspecific reactive changes such as mild gliosis or edema. In addition, a thorough investigation to rule out opportunistic infections should be performed for the diagnosis of rheumatoid meningitis, because intensive immunotherapy is often needed for its treatment. Pathogens causing CNS infection in patients with rheumatoid arthritis include *M tuberculosis*, *Cryptococcus*, and *Listeria*.8–10

Concurrently, it should be kept in mind that IgG4-related hypertrophic pachymeningitis (IgG4-RHP), an increasingly recognized CNS manifestation of IgG4-related disease (IgG4-RD), is a fibroinflammatory disease often leading to asymmetric or localized dural thickening. As the exact pathogenesis of IgG4-RD remains unclear, collaboration between CD4-positive T cells and activated, somatically hypermutated IgG4-positive plasmablasts might be a key pathophysiologic mechanism.1,2,3 The characteristic histopathologic features of IgG4-RD are dense lymphoplasmacytic infiltrates, storiform fibrosis, and obliterator phlebitis.1,2,3 As the name of IgG4-RHP implies, IgG4-RD has a predilection for the pachymeninges in the CNS.4–6,5 Therefore, it is desirable to consider IgG4-RD as a differential diagnosis when the pachymeninges are asymmetrically involved. However, because several case reports also demonstrated IgG4-related leptomeningitis,6–8 IgG4-RD could be considered, although less likely, as a differential diagnosis in cases of asymmetric leptomeningitis. In addition, granulomatous diseases such as granulomatosis with polyangiitis, neurosarcoidosis, neurosyphilis, and meningeal metastasis are all important considerations in the differential diagnosis of rheumatoid meningitis.9–11

The reasons for a meningeal, rather than brain parenchymal, predilection in rheumatoid meningitis, and the pathophysiology of its asymmetric meningeal involvement, remain unclear. One possible explanation is that autoimmunity against collagen fiber, a major component of the meninges, and its contiguous spreading may play a pathogenic role. The precise mechanisms of asymmetric meningeal involvement require further investigation.

Rheumatoid meningitis can be one of the important differential diagnoses in a patient with rheumatoid arthritis and asymmetric or unilateral neurologic symptoms. Although a meningeal biopsy is necessary to confirm the diagnosis, a common MRI feature of asymmetric meningeal involvement may lead to earlier diagnosis of rheumatoid meningitis. Nonetheless, an extensive evaluation to exclude opportunistic infections of the CNS must be conducted before a diagnosis is made.

**AUTHOR CONTRIBUTIONS**

Seok-Jin Cho: design and conceptualization of the study, analysis and interpretation of the data, drafting and revising the manuscript. Young Ho Park: design and conceptualization of the study, analysis and interpretation of the data, revising the manuscript. Jin Ah Kim: analysis and interpretation of the data, revising the manuscript. Jung Ho Han and Gheesyong Cho: analysis and interpretation of the data. SangYun Kim: analysis and interpretation of the data, revising the manuscript.

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**DISCLOSURE**

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

**REFERENCES**

Residency Training

These manuscripts will address issues related to residency training, including educational initiatives, programs, opinions, and other topics related to neurology education and training. Relevant topics could include work hours and sleep deprivation, the role of neurocritical care or outpatient neurology in training, quality assurance initiatives, incorporation of evidence-based neurology into training, medical student teaching, work/life balance, and others. Seeking the assistance of senior faculty members is often useful.
Residency Training: The need for an integrated diversity curriculum for neurology residency

ABSTRACT

Background: Providing culturally responsive care to an increasingly multicultural population is essential and requires formal cultural humility training for residents. We sought to understand the current prevalence and need for this type of training within neurology programs and to pilot an integrated curriculum locally.

Needs assessment: We surveyed via email all program directors of academic neurology programs nationally regarding the prevalence of and need for formal cultural responsiveness training. Forty-seven program directors (36%) responded to the survey. The majority of respondents did not have a formalized diversity curriculum in their program (65%), but most (85%) believed that training in cultural responsiveness was important.

Program description: We developed locally an integrated diversity curriculum as a proof of concept. The curriculum covered topics of diversity in language, religion, sexual orientation, gender identity/expression, and socioeconomic status designed to focus on the needs of the local community. Program evaluation included a pre and post survey of the learner attitudes toward cultural diversity.

Future directions: There is an unmet need for cultural responsiveness training within neurology residencies, and integrating this curriculum is both feasible and efficacious. When adapted to address cultural issues of the local community, this curriculum can be generalizable to both academic and community organizations. Neurology® 2017;89:e284–e287

GLOSSARY

LGBT = lesbian, gay, bisexual, or transgender; UCSF = University of California, San Francisco.

The landscape of medical practice is changing, including the diversity of the communities in which we practice. Juxtaposed to these cultural changes are persistent disparities in neurologic disease outcomes, including stroke, movement disorders, and headache.1–3

While the etiology of disparities is multifactorial, some have suggested that provider behavior is a significant contributing factor,4,5 highlighting the importance of training in providing culturally responsive care. Although some medical schools have integrated formal cultural responsiveness training, this is by no means standard.6 Trainees arrive to residency with a wide variety of experience in navigating how culture influences a patient–physician rapport and have the potential to magnify existing disparities in access to equitable care.

Diversity curriculum interventions have been implemented in some specialties;7,8 however, there has yet to be a formal evaluation of the state of cultural responsiveness training in neurology. We therefore performed a needs assessment of residency programs nationally, and then sought to address this curricular gap locally by creating a program both as a proof-of-concept exercise and to serve as a blueprint that could be replicated nationally.

For the purposes of this article and the curriculum, diversity was defined broadly to include sex, race/ethnicity, religion, sexual orientation, gender identity/expression, socioeconomic status, and ability. In addition, cultural responsiveness, cultural competence, and cultural humility were used synonymously, although they each have distinct formal meanings.

All aspects of this study were approved by the institutional review board of the University of California, San Francisco (UCSF).

NEEDS ASSESSMENT A 27-question anonymous questionnaire was emailed to the program directors of
all accredited US neurology training programs (see supplemental material e-1 at Neurology.org) obtained through the Accreditation Council for Graduate Medical Education for 2015–2016. A portion of the questionnaire was adapted from the UMDNJ-Robert Wood Johnson Clinical Cultural Competency Questionnaire with permission.9

The survey queried if a formalized curriculum for cultural responsiveness was in place or in development, how important this training is in the estimation of the program directors, and explored barriers to implementation.

A total of 47 program directors (36%) responded to the survey, with an average program size of 11–20 residents across the PGY2-PGY4 years. The highest proportion of respondents were located in the Southeast (n = 9; 56% of programs in that geographic area), followed by the West (n = 9; 43%), Midwest (n = 11; 42%), Northeast (n = 15; 34%), and South (n = 3; 13%).

The majority of program directors believed that training in cultural responsiveness was important (n = 30; 85%), but most did not have a formalized diversity curriculum in their program (n = 24; 65%), although some programs (n = 7; 19%) had curricula in development. Time, lack of expertise, and lack of educational materials were the most commonly cited barriers to formalized training.

PROGRAM OBJECTIVES: The objective of the local curriculum was twofold: to bring awareness to trainees about topics that affect the local community and influence their relationship with the health care system and to assess the efficacy and feasibility of integrating this type of curriculum within a neurology residency. With the first goal in mind, the curriculum was tailored to address cultural issues that arise in caring for the community in San Francisco. For example, since the majority of patients cared for within our county hospital speak a primary language other than English, we addressed language as an instrument of culture and focused on medical interpretation skills. There is also a large San Francisco community who identify as lesbian, gay, bisexual, or transgender (LGBT), so we ensured that trainees were comfortable with terminology and specific health concerns of this community.

A before and after survey of the learners was administered in which they were asked to assess their skill and comfort in navigating clinical scenarios using a 5-point Likert scale (see supplemental material e-2). Residents were also asked about the importance of health professionals receiving formal training in cultural humility. Prior exposure to formal multicultural training prior to residency was assessed. The same survey was distributed at the end of the curriculum to assess for any change and to ask for feedback on the curriculum and recommendations for future topics. Results were analyzed using the rank sum test.

PROGRAM DESCRIPTION: The curriculum was given to UCSF neurology residents and comprised six 1-hour lectures scheduled during weekly resident didactic sessions.

The series was broken down into themes. The first lecture served to provide context for the curriculum and focused on the presence of unconscious bias in medical decision-making and in health care interactions. Prior to the lecture, the residents were asked to complete 2 of the Harvard Implicit Association Tests to engage in processing their own unconscious biases.10

The next series of lectures focused on diversity in ethnicity, language, and religion. A panel of religious leaders from the local community discussed how religious beliefs interplay with medical care, particularly in regards to end-of-life discussions. In another session, an interpreter addressed difficult discussions with patients and families, and how skill in interpreter use can bridge cultural divides.

The next lectures focused on LGBT health. The first defined sexual orientation and gender identity terms and discussed the current knowledge of disparities that influence neurologic disease in this population. The second focused specifically on transgender health and identity, particularly in relation to gender-affirming hormones and risk for neurologic disorders.

The series culminated in a Grand Rounds lecture, attended by faculty, staff, and trainees, and part of an annual diversity series, in which an expert in socioeconomic determinants of health spoke on the role of stress and early childhood experiences in perpetuating socioeconomic disparities in health.

PROGRAM EVALUATION AND FEEDBACK: A total of 24 residents (53%) responded to the precurriculum survey. The majority had undergone some previous formal training in cultural responsiveness: 17% reported no formal training and 54% some training in college, while 54% reported monthly or more frequent training in medical school. Prior to the start of the curriculum, most residents believed that it was important for health professionals to receive formal training in cultural responsiveness (mean 4.42 out of 5.0, where 5.0 was “extremely important”).

Twenty residents (44%) responded to the postcurriculum survey. Of these, the majority attended at least one of the lectures in the diversity curriculum series. Residents reported significantly improved understanding of the role of implicit bias in medical
decision-making (3.08 vs 3.68; \(p = 0.01\)), significantly improved appreciation of transgender health issues (2.54 vs 3.4; \(p = 0.003\)), and significantly more skill in both understanding how an individual’s disability affects his or her health care (2.97 vs 3.63; \(p = 0.009\)) and in assessing a patient’s medical literacy (3.08 vs 3.6; \(p = 0.044\)). In addition, residents felt significantly more comfortable apologizing for cross-cultural errors (3.375 vs 3.8; \(p = 0.048\)), significantly more comfortable pronoun for gender identification (2.95 vs 3.6; \(p = 0.017\)), and significantly more comfortable counseling a patient with limited English proficiency (3.54 vs 4.1; \(p = 0.016\)). After completion of the curriculum, residents continued to feel strongly that formal training in cultural responsiveness was important (mean 4.32; \(p = 0.62\)).

Comments suggested that the curriculum was interesting, relevant, and beneficial. Comments included that they “don’t get enough of this in the (hospital)” and that “it is a gift to have this training early on” in their careers.

**LESSONS LEARNED** In developing the local diversity curriculum, we stressed the importance of connecting the material directly to clinical care by using examples from cases that trainees have experienced or by providing concrete tools that they can use going forward. Tailoring the curriculum to the demographics and needs of the local community is essential.

Another important lesson was tailoring the evaluation to the objectives of the curriculum. For example, although we asked about self-reported confidence, this does not necessarily indicate improved cultural humility; perhaps evaluations should focus more on an objective measure of communication (such as a standardized patient) or patient satisfaction.

**FUTURE DIRECTIONS** Given that lack of materials and lack of expertise were 2 of the top barriers cited to implementing a diversity curriculum, we are now developing a standardized curriculum modeled after ours, available for dissemination and modification nationally. The local curriculum has also continued. In upcoming years, we hope to more fully integrate culturally responsive topics within the traditional didactics (e.g., when there is a lecture on stroke, incorporating information about LGBT health and risk of stroke). We also hope to integrate patient satisfaction and outcomes into the evaluation process to determine the direct effect of the curriculum.

There are many possibilities for future directions (table), which can be tailored to the needs of a particular local patient population. As this conversation develops, the focus can shift from an ideology of cultural competence, which suggests a set curriculum that can be mastered, to cultural humility, which encourages self-reflection and lifelong learning. Through this growth, we will be more equipped to address the pervasive disparities that affect the lives of our patients and move toward providing more equitable care for all.

**AUTHOR CONTRIBUTIONS**

Nicole Rosendale: study conceptualization, drafting and revision of the manuscript. S. Andrew Josephson: study conceptualization, revision of manuscript, supervision of the study.

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**Table Possible future directions for neurology curriculum on cultural awareness**

<table>
<thead>
<tr>
<th>Theme</th>
<th>Possible didactic topics/formats</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Context for the curriculum</strong></td>
<td>Discussion of unconscious bias</td>
</tr>
<tr>
<td></td>
<td>Discussion of socioeconomic determinants of health</td>
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<tr>
<td></td>
<td>Microaggressions and imposter syndrome in medicine</td>
</tr>
<tr>
<td></td>
<td>Discussion of identity and privilege</td>
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<tr>
<td></td>
<td>Discussion of identity and intersectionality</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td>Racial/ethnic disparities in stroke</td>
</tr>
<tr>
<td></td>
<td>Racial/ethnic disparities in epilepsy</td>
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<tr>
<td></td>
<td>Racial/ethnic disparities in quality measures/outcomes</td>
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<tr>
<td></td>
<td>Patient panel on experiences of discrimination in health care</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td>Panel of community leaders discussing interplay of faith and medicine</td>
</tr>
<tr>
<td></td>
<td>Patient panel discussing importance of religion in medical decision making</td>
</tr>
<tr>
<td><strong>Socioeconomic status</strong></td>
<td>Discussion of socioeconomic disparities in neurologic disease outcomes</td>
</tr>
<tr>
<td></td>
<td>Discussion of available services for marginally housed/homeless individuals in the local community</td>
</tr>
<tr>
<td><strong>Ability</strong></td>
<td>Discussion of available disability services in the area and how to connect patients to those services</td>
</tr>
<tr>
<td></td>
<td>Presentation by disability rights group on local issues</td>
</tr>
<tr>
<td></td>
<td>Panel of patients discussing how their disability affects their daily life and interaction with the health care system</td>
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<tr>
<td><strong>Sexual orientation</strong></td>
<td>Patient panel discussing instances of discrimination in the health care system</td>
</tr>
<tr>
<td></td>
<td>Introduction of terminology and disparities in lesbian, gay, bisexual, or transgender health</td>
</tr>
<tr>
<td><strong>Gender identity</strong></td>
<td>Defining sexual orientation vs gender identity/expression</td>
</tr>
<tr>
<td></td>
<td>Discussion of navigating the world as a gender nonconforming individual</td>
</tr>
<tr>
<td></td>
<td>Discussion of available gender-affirming therapies and neurologic implications</td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>Discussion of when and how to use medical interpreters</td>
</tr>
<tr>
<td></td>
<td>Standardized patient as a way of practicing skills of using a medical interpreter</td>
</tr>
<tr>
<td><strong>Integrative medicine</strong></td>
<td>Discussion of use of acupuncture in treatment of pain</td>
</tr>
<tr>
<td></td>
<td>Discussion of complementary methods of addressing neurologic disease (i.e., tai chi for Parkinson disease)</td>
</tr>
</tbody>
</table>
evaluation survey; and John Engstrom, MD (University of California San Francisco), for supporting integration of cultural responsiveness training in the existing neurology resident didactic sessions.

STUDY FUNDING
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REFERENCES

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Right Brain

Right Brain is a feature devoted to the relationship between neurology and the medical humanities, with submissions either written by trainees or with a focus on the experience of the trainee. Appropriate submissions include articles, commentaries, and reflections on the interaction between neurology and history, literature, ethics, theology, sociology, anthropology, philosophy, poetry, theater, film, fine arts, or the media. Right Brain also will publish original works of fiction, poetry, and reflection written by residents and fellows relating to the practice of neurology or neurology training.
Right Brain: The fragile sense of self in neurodegenerative disease

A brief philosophical examination

This essay was selected as the winner of the American Academy of Neurology’s CNRF Essay Contest.

Progressive neurodegenerative diseases such as Alzheimer disease, Parkinson disease, and Huntington disease are all associated with cognitive decline that may eventually result in advanced dementia and loss of the many elements that contribute to consciousness and self-awareness. This is a confronting prospect for many people living with these diseases, their families, and society as a whole.

The concepts of self-awareness and consciousness are notoriously elusive brain functions to define. They are not only practical neurologic descriptors but also terms that are widely used in the literature, philosophy, and psychology. Consciousness may be practically defined by the physician as “the state of awareness of self and environment, and responsiveness to external stimulation and inner need.” This requires the normal functioning of several facets of the nervous system for the integration and association of multiple sensory, motor, and emotional inputs into a single unified percept. Philosophical perspectives can inform the discussion of self and self-awareness in neurodegenerative disease and may contribute to the foundation of a more positive approach.

Neurodegenerative diseases are characterized by the insidious, rather than sudden, loss of mental faculties. This is a challenge for patients, families, and professionals as there is no definable moment in which a person loses their self-awareness, agency, and purpose, but this is, rather, a gradual process. Alzheimer disease is characterized by the early emergence of a significant and progressive episodic memory deficit. This may be associated with other cognitive deficits including neuropsychiatric changes, executive and language dysfunctions, and visual processing impairments. Dementia is also common in Parkinson disease and may be termed Parkinson disease dementia (PDD) when it is preceded by the clinical motor features of Parkinson disease by at least 1 year or dementia with Lewy bodies (DLB) when dementia occurs simultaneously or within 1 year of motor parkinsonism. Other core features of DLB include well-formed visual hallucinations, cognitive fluctuations, and sleep disturbance. Finally, Huntington disease typically presents with the combination of a movement disorder and a frontal dementia characterized by a range of psychiatric and cognitive symptoms. Individuals with Huntington disease develop prominent cognitive deficits on tests of attention, semantic verbal fluency, processing speed, and executive function. All of these diseases are associated with varying degrees of anosognosia. This further compromises self-awareness by creating a disconnect between the internal and external projections of self.

While dementia represents the gradual erosion of cognitive capacity and self-awareness, the state of delirium illustrates that this can also be a dynamic construct. Those with neurodegenerative disease are at higher risk of developing delirium, which can simply be defined as an acute confusional state typically affecting older people with an acute medical illness. One criterion for a diagnosis of delirium is a fluctuating course, and therefore, individuals’ degree of self-awareness and cognitive capacity may vary greatly within the course of a single day. Notably, cognitive fluctuations are also typical of those with DLB.

Much of Western philosophy is premised on the intact mind. For example, Descartes famously concluded, “I think, therefore I am” and conceived a sharp separation between the mind and body, termed Cartesian dualism. By extension, those individuals with advanced dementia who are no longer capable of rational thought could be considered not to exist. Cartesian dualism implies that the mind can outlive the body, but in dementia, many would say that the converse is true. Certainly, caregivers of those with dementia report that the loss of “personhood” and “social death” predate biological death.

John Locke, the philosopher, conceived a thought experiment in his discussion of personal identity:

For should the soul of a prince, carrying with it the consciousness of the prince’s past life, enter and inform the body of a cobbler, as soon as deserted by his own soul, every one sees he would be the same person with the prince, accountable only for the prince’s actions: but who would say it was the same man?
In this scenario, it would not be fair to hold the man with the body of the prince responsible for the prince’s former actions as he would have no recollection of performing them. This is an interesting notion in relation to dementia. It is perhaps fortunate that long-term autobiographical memory is usually lost late in the course of the disease as this appears integral to individual identity. However, in advanced dementia, when, for instance, people are no longer able to recognize even their siblings, it may be fair to say that they are only faint facsimiles of the individuals they used to be.

Kant conceptualized individuals as rational beings who are capable of leading their own lives and therefore we should accept their autonomy. This relates to one of the commonest ethical dilemmas facing doctors treating those with cognitive decline. It can be difficult to define the point at which it becomes morally acceptable to deny individual autonomy to people who have lost the capacity for rational thought. For Kant, persons are rational beings, and therefore, those who have lost the capacity for rational thought are no longer persons. However, this has been challenged by Kitwood and others. Kitwood’s notion of person-centered care for dementia, emphasizing the essential humanity of the person rather than the disease and its deficits, is crucial to the maintenance of dignity and “personhood.”

While there have been developments in our understanding of dementia and resources are directed toward the development of potential treatments, most types of dementia remain incurable. The prospect of losing one’s mental faculties and the inevitable progressive decline culminating in death is an understandably challenging one for most people. With advances in other areas of medicine and increasing life expectancies, particularly in the Western world, these issues will become more prominent.

Aldous Huxley provides a particularly graphic solution for those confronted by the idea of aging and dying in his dystopian novel *Brave New World*. At the “Park Lane Hospital for the Dying,” middle-aged people accelerate through their later years and into a state of second infancy soothed by the ubiquitous psychotropic drug *soma*. While this is an extreme fictional account of a possible future, there are nevertheless uncomfortable comparisons to be drawn with some modern nursing homes in which those with neurodegenerative diseases are kept safely away from the majority of society and pacified with multiple psychotropic medications. It is perhaps no surprise that people kept in these artificial environments and denied their autonomy can become depressed, angry, or even violent and be transferred back to acute hospital environments that are, in some ways, even more dehumanizing.

Two ideas that may be comforting in the face of such devastating diseases and the social isolation they may portend are derived from Buddhism and the work of the Austrian psychiatrist Victor Frankl. Contrary to much of Western philosophical thought, the Buddha taught that “you” are not an integral autonomous entity. If we can see through the delusion of attachment to an individual self, we experience that which is not subject to birth and death. A logical extension of this idea is that we are part of a broader society. Working to integrate those with neurodegenerative disease into the society rather than ostracizing and isolating them in institutions may have practical advantages for these individuals. This relates both to those still living in the community with varying degrees of independence and to those who have been institutionalized. In addition, for the broader society, exposure to people with such conditions may go some way to ameliorating the fear of the unknown.

Victor Frankl’s experiences as a Jew incarcerated in a concentration camp during the second world war inspired him to write “Man’s Search for Meaning” and develop logotherapy. Frankl determined that in order to survive, one must have optimism in the face of tragedy and in view of human potential. He conceived that the search for meaning should be the primary motivation in life and that there is an inherent but largely constructive tension between “...what one has already achieved and what one still ought to accomplish....” This philosophy can also be applied to human suffering, with Frankl writing:

...[W]e may also find meaning in life even when confronted with a hopeless situation, when facing a fate that cannot be changed. For what then matters is to bear witness to the uniquely human potential at its best, which is to transform a personal tragedy into a triumph, to turn one’s predicament into a human achievement.

This concept is readily translatable to those living with neurodegenerative disease. Finding meaning in life and ensuring that people still engage in meaningful activities even at a stage at which they are profoundly disabled can only be a positive endeavor.

The prospect of losing oneself with the inevitable progression of a neurodegenerative disease associated with cognitive decline is a daunting one, and there are a wealth of philosophical ideas that relate to this predicament. While some reinforce the notion of “social death” and loss of “personhood,” hope can also be derived from the Buddhist notion of letting go of the “self” and enabling these individuals to be better integrated into society. Lastly, finding meaning in life allows those with neurodegenerative disease to remain positive and correspondingly bolsters their resilience.

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Teaching NeuroImages: Sonographic detection of intraneural perineurioma in therapy-refractory carpal tunnel syndrome

A 55-year-old man with typical clinical and electrodiagnostic findings of carpal tunnel syndrome complained of progression of his symptoms. Since repeated surgical interventions did not provide any relief, sonographic examination was performed and depicted a massive median nerve enlargement with hyperechoic perineurial tissue (figure, A). Beyond postoperative perineural fibrosis, the findings were suspicious for an underlying tumor. MRI revealed a tumorous nerve swelling and surgical neurolysis of hypertrophic fascicles followed (figure, B and C). Histopathology confirmed the diagnosis of intraneural perineurioma, a rare, benign, slow-growing peripheral nerve sheath tumor of perineurial cell origin (figure, D and E).1 Nerve sonography is recommended in therapy-refractory cases, as it might uncover unusual causes of entrapment syndromes.2

AUTHOR CONTRIBUTIONS
Christos Krogias: drafting the manuscript, acquisition of data, analysis and interpretation of data. Ralf Gold: revising the manuscript, analysis and interpretation of data. Thomas Schelle: revising the manuscript, analysis and interpretation of data. Josef Böhm: revising the manuscript, analysis and interpretation of data. Andreas Junker: revising the manuscript, acquisition of data, analysis and interpretation of data. Ulrich Sure: revising the manuscript, analysis and interpretation of data. Ann-Kathrin Uerschels: revising the manuscript, acquisition of data, analysis and interpretation of data, study concept or design. All authors read and approved the content of the manuscript.

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REFERENCES
Figure Multimodal imaging and diagnosis of perineurioma

(A) Sonography reveals enlarged nerve (encircled area, 0.58 cm²) at wrist. (B) T1-weighted MRI depicts enlarged fascicles (black arrow). White arrow: tendons. (C) Resection of epineural sheet reveals tumorous transformation of fascicles with perineural swelling (asterisk). (D) Hematoxylin & eosin stain: intrafascicular tumor cells surrounded by collagen fibers. (E) Epithelial membrane antigen–stained positive tumor cells.

(A) Sonography reveals enlarged nerve (encircled area, 0.58 cm²) at wrist. (B) T1-weighted MRI depicts enlarged fascicles (black arrow). White arrow: tendons. (C) Resection of epineural sheet reveals tumorous transformation of fascicles with perineural swelling (asterisk). (D) Hematoxylin & eosin stain: intrafascicular tumor cells surrounded by collagen fibers. (E) Epithelial membrane antigen–stained positive tumor cells.
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