Annual Highlights of the Resident & Fellow Section: 2016

A Representative Collection of Previously Published Articles
Navigating Your Career: ALL ABOARD!

Friday, April 15–Thursday, April 21, 2016

Vancouver Convention Centre, West Level 2

Learn about career development at every stage: from “choosing a track,” to “staying on track,” to “changing tracks” in your career. This area has something for everyone: medical students, residents, fellows, junior faculty, senior faculty, and advanced practice providers.

- Learn from successful neurologists and advanced practice providers on how to establish and maintain effective partnerships
- Hear from neurologists who chose careers outside of academia in areas such as teleneurology, government, and advocacy
- Hone your skills in conflict resolution, giving and receiving feedback, and interviewing

Faculty and Trainee Reception

Saturday, April 16

Vancouver Convention Centre West, Level 1, Ballroom C&D

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. Meet the Neurology Residents & Fellows Section editors and editorial team at the R&F booth.
# Table of Contents

1. **RESIDENTS & FELLOWS SECTION EDITORIAL TEAM**

   John J. Millichap, Roy E. Strowd, Kathleen Pieper

4. **TOP 10 WAYS FOR PROGRAM DIRECTORS TO USE THE NEUROLOGY RESIDENT & FELLOW SECTION**  
   Sara Stern-Nezer, John J. Millichap, Roy E. Strowd

5. **2016 R&F WRITING AWARD WINNER**

6. **E-PEARLS OF THE WEEK**  
   A. Numis and J. Addington

7. **CHILD NEUROLOGY**  
   8. **Andersen-Tawil syndrome**  
      M. Almuqbil and M. Srour | March 17, 2015 84: e78-e80

11. **CLINICAL REASONING**  
   12. **A 56-year-old man with cognitive impairment and difficulty tying his necktie**  

17. **EDUCATION RESEARCH**  
   18. **A case-based bioethics curriculum for neurology residents**  

21. **EMERGING SUBSPECIALTIES IN NEUROLOGY**  
   22. **2016 Award Winner! Telestroke and teleneurology**  
       S. Mutgi, Alicia Zha, and R. Behrouz | June 2, 2015 84: e191-e193

25. **INTERNATIONAL ISSUES**  
   26. **An international survey of young neurologists’ perceptions of future health care and neurology**  

30. **JOURNAL CLUB**  
   31. **Randomized phase III study of whole-brain radiotherapy for primary CNS lymphoma**  
       I. Alnahhas and M. Malkin | December 15, 2015 85: e187-e189

34. **MEDIA AND BOOK REVIEWS**  
   35. **Reaching Down the Rabbit Hole: Extraordinary Journeys into the Human Brain**  
       P.A. Kempster | December 15, 2015 85: e193

36. **MYSTERY CASE**  
   37. **A 21-year-old man with visual loss following marijuana use**  

42. **OPINION & SPECIAL ARTICLES**  
   43. **An interdisciplinary neuroinfectious diseases clinic to improve patient care and training**  
       F.C. Chow, B.S. Schwartz, and S.A. Josephson | January 6, 2015 84: e1-e4

47. **PEARLS AND OY-STERS**  
   48. **Pisa syndrome: An unusual feature of adult-onset fulminant SSPE**  

51. **RESIDENCY TRAINING**  
   52. **Determinants of burnout of neurology trainees in Attica, Greece**  
       P. Zis, A. Artemiadis, M. Lykouri, S. Xiou, A. Roussopoulou, E. Papageorgiou, E. Bakola, and F. Anagnostopoulos | September 15, 2015 85: e81-e84

56. **TEACHING NEUROIMAGES**  
   57. **The lentiform fork sign: An MRI pattern of metformin-associated encephalopathy**  

58. **TEACHING VIDEO NEUROIMAGES**  
   59. **Feeding dystonia in chorea-acanthocytosis**  
       M. Paucar, P-A Lindestad, R.H. Walker, and P. Svenningsson | November 10, 2015 85: e143-e144

---

*About the Cover:* FDG-PET shows right greater than left hypometabolism in the basal ganglia, temporal lobes, and parietal lobes. From the article: Clinical Reasoning: A 56-year-old man with cognitive impairment and difficulty tying his necktie by Jessica M. Baker, MD; Joel Salinas, MD, MBA; and Aaron L. Berkowitz, MD, PhD. See page 12.
Roy E. Strowd, MD

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 his 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 with support from 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.

Ingo Helbig, MD

Ingo Helbig is a child neurology fellow at Children’s Hospital Los Angeles. He graduated from Pomona College in Claremont, CA. She went on to the University of California, San Francisco before attending medical school. She graduated from the Keck School of Medicine and completed her pediatric training at Children’s Hospital Los Angeles. She will begin a neuroimmunology fellowship at UCSF in 2015.

Aravind Ganesh, MD

Aravind Ganesh is a senior neurology resident at the University of Calgary. He is currently pursuing a DPhil in clinical neurosciences on a Rhodes scholarship at Oxford’s Centre for Clinical Neurosciences. He serves as junior dean and clinical teaching associate at St John’s College, Oxford, and has cofounded SnapRx, a point-of-care mHealth venture.

Jen Cialone, MD

Jen Cialone is a child neurology resident at University of Rochester Medical Center in Rochester, NY. She obtained her bachelor’s degree in molecular and cellular biology from Vanderbilt University in Nashville, TN. She obtained her MD from University of Rochester School of Medicine and Dentistry, where she also did research on Batten’s Disease.

Carla Francisco, MD

Carla Francisco is a child neurology fellow at Children’s Hospital Los Angeles. She graduated from Pomona College in Claremont, CA. She went on to the University of California, San Francisco before attending medical school. She graduated from the Keck School of Medicine and completed her pediatric training at Children’s Hospital Los Angeles. She will begin a neuroimmunology fellowship at UCSF in 2015.

Kristen Lindgren, MD, PhD

Kristen Lindgren is a third-year child neurology resident at the Children’s Hospital of Philadelphia and has transitioned to the US after completing a German pediatrics fellowship. She has attended the University of Heidelberg Medical School and University of Kentucky, Lexington. He has a strong interest in neurogenetics, particularly epilepsy genetics, and is an avid blogger on Beyond the Ion Channel at Epilepygenetics.net.

Jonathan T. Kleinman, MD

Jonathan Kleinman is chief neurology resident at University of California, Los Angeles. He obtained his bachelor’s degree from The Johns Hopkins University in cellular and molecular neuroscience, and his medical degree from Stanford University. He will begin fellowship in neurocritical care at UCLA starting July 2016.

Samuel Lapalme-Remis, MD, MA, FRCP
gaturaltext

Samuel Lapalme-Remis is a first-year fellow in clinical neurophysiology EEG and epilepsy at Mayo Clinic in Rochester, MN. He completed his MD at McGill University and his residency in adult neurology at the University of Ottawa. Prior to medical school, he worked in Japan for several years. His academic interests include epilepsy, sleep, 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.

He completed his DPhil at the University of Oxford, where he studied the genetics of multiple sclerosis. Current research interests include multiple sclerosis and the history of neurology.

Emer McGrath, MD, PhD, MRCP

Emer McGrath is an adult neurology resident at MGH and Brigham and Women’s Hospital Partners Neurology program. She completed her MD and PhD at the National University of Ireland. She trained in clinical epidemiology and biostatistics during her PhD—her current research focuses on epidemiology of stroke, vascular disease and dementia.

John J. Millichap, MD, FAAP

John Millichap is a pediatric epileptologist in the Comprehensive Epilepsy Center at Ann and Robert H. Lurie Children’s Hospital of Chicago and an Assistant Professor of Pediatrics and Neurology at Northwestern University Feinberg School of Medicine. He also serves as chief resident at the Brody School of Medicine at East Carolina University. Millichap is an avid writer and enjoys encouraging resident and fellow contributions to the medical literature.
Sarah Flanagan Wesley, MD
Sarah Flanagan Wesley graduated from the Royal College of Surgeons in Ireland, where she served as president of the RCS Society of Neuroscience. She earned a BA in English literature from Davidson College, an MPH from Dartmouth’s Institute for Health Policy and Clinical Practice, and has contributed to other educational publications, including First Aid for the USMLE. Currently, she serves as chief resident of neurology at Mount Sinai Beth Israel in New York City. Upon completion of her residency, she will be starting a fellowship at Yale-New Haven Hospital in clinical neuroimmunology/MS.

Michael White, MD
Michael White graduated from Lake Forest College in 2007 and received his MD from the University at Buffalo in 2012. He is currently a neurology resident at Washington University in St. Louis, where his research interests include developing and implementing phase I and II clinical trials for new chemotherapeutics in high-grade glial tumors. He is also interested in utilizing MRI and quantitative MRI-perfusion imaging in addition to genetic markers to assess disease status in glioblastoma. He plans to pursue fellowship training in neuro-oncology. Outside of medicine, he plays on an ice hockey team and is an avid road bicyclist.

Khaled Moussawi, MD, PhD
Khaled Moussawi is an adult neurology resident at the Partners Neurology program. He attended the American University of Beirut in Lebanon for his undergraduate studies. He then completed his MD and PhD degrees at the Medical University of South Carolina. His research focused on understanding the motivational circuits in addiction. He is interested in neuropsychiatry and cognitive neurology in addition to novel diagnostic approaches in neurology.

Adam Numis, MD
Adam Numis is a child neurology fellow at the University of California, San Francisco. He is a graduate of Harvard Medical School and completed his pediatric training at Boston Children’s Hospital/Boston Combined Residency Program. His academic interests include epidemiological and translational investigations in pediatric epilepsy and neurocritical care. He also has an interest in issues related to advocacy and education.

Steve O’Donnell, MD
Steve O’Donnell attended the University of Rochester for both his undergraduate and medical education. He is currently at the University of Utah and will finish his residency in adult neurology in 2017. He plans to pursue a fellowship in vascular neurology and to integrate international work into his future career.

Craig Press, MD, PhD
Craig Press is a pediatric neurocritical care fellow at Ann & Robert H. Lurie Children’s Hospital of Chicago. He received his MD/PhD from Washington University in St. Louis, and completed child neurology training in Denver. He is now focusing on using big data to improve patient outcomes and quantitative EEG for neurocritical care.

Andrew Sas, MD, PhD
Andrew Sas is a neurology resident at the University of Michigan. He completed his BS in biology at Dickinson College. He then attended the Medical University of South Carolina, where he completed his MD and PhD studying neuroimmunology. His current academic interests include clinical care and translational research in the area neuroimmunology of traumatic brain injury and sports neurology.

Raphael Schneider, MD
Raphael Schneider is currently a fourth-year neurology resident at the University of Toronto, Canada. Originally from Germany, he attended medical school at the Albert-Ludwigs Universität of Freiburg. He then completed a postdoctoral fellowship at the Université de Montréal, Canada, with a research focus on the immunobiology of multiple sclerosis. Future areas of exploration include neuroinflammation and motor neuron disease.

James Siegler, MD
James Siegler is an adult neurology resident at UPenn. He graduated from The Johns Hopkins University with degrees in neuroscience and history of medicine prior to completing his MD at Tulane. When he is not carrying out research, he is biking, playing with his dog, or conceiving ways to retire in the Caribbean.

Khaled Moussawi, MD, PhD
Khaled Moussawi is an adult neurology resident at the Partners Neurology program. He attended the American University of Beirut in Lebanon for his undergraduate studies. He then completed his MD and PhD degrees at the Medical University of South Carolina. His research focused on understanding the motivational circuits in addiction. He is interested in neuropsychiatry and cognitive neurology in addition to novel diagnostic approaches in neurology.

Adam Numis, MD
Adam Numis is a child neurology fellow at the University of California, San Francisco. He is a graduate of Harvard Medical School and completed his pediatric training at Boston Children’s Hospital/Boston Combined Residency Program. His academic interests include epidemiological and translational investigations in pediatric epilepsy and neurocritical care. He also has an interest in issues related to advocacy and education.

Steve O’Donnell, MD
Steve O’Donnell attended the University of Rochester for both his undergraduate and medical education. He is currently at the University of Utah and will finish his residency in adult neurology in 2017. He plans to pursue a fellowship in vascular neurology and to integrate international work into his future career.

Craig Press, MD, PhD
Craig Press is a pediatric neurocritical care fellow at Ann & Robert H. Lurie Children’s Hospital of Chicago. He received his MD/PhD from Washington University in St. Louis, and completed child neurology training in Denver. He is now focusing on using big data to improve patient outcomes and quantitative EEG for neurocritical care.

Andrew Sas, MD, PhD
Andrew Sas is a neurology resident at the University of Michigan. He completed his BS in biology at Dickinson College. He then attended the Medical University of South Carolina, where he completed his MD and PhD studying neuroimmunology. His current academic interests include clinical care and translational research in the area neuroimmunology of traumatic brain injury and sports neurology.

Raphael Schneider, MD
Raphael Schneider is currently a fourth-year neurology resident at the University of Toronto, Canada. Originally from Germany, he attended medical school at the Albert-Ludwigs Universität of Freiburg. He then completed a postdoctoral fellowship at the Université de Montréal, Canada, with a research focus on the immunobiology of multiple sclerosis. Future areas of exploration include neuroinflammation and motor neuron disease.

James Siegler, MD
James Siegler is an adult neurology resident at UPenn. He graduated from The Johns Hopkins University with degrees in neuroscience and history of medicine prior to completing his MD at Tulane. When he is not carrying out research, he is biking, playing with his dog, or conceiving ways to retire in the Caribbean.
The Resident & Fellow Section

John J. Millichap, Roy Strowd, Kathleen Pieper

The Resident & Fellow “Page” was launched in 2004 as a forum for trainees and educators to publish articles on topics relevant to residency and fellowship. Initially lead by Robert “Berch” Griggs, then the editor-in-chief of Neurology®, and Karen Johnston, associate editor, the article types included clinical reviews and education research projects, as well as commentaries on practice, ethics, teaching, history, and international training experiences. By 2015, with the guidance of Mitch Elkind, the “Page” had grown to a “Section,” with articles appearing weekly, projects like Podcasts and the Writing Award, and a growing team of editorial members.

The Resident & Fellow Section (RFS) is trainee-run: A nationally representative team of more than 20 residents and fellows, each of whom serves three years, has responsibility for reviewing, editing, and publishing articles. Residents are selected annually, through a competitive process that attracts dozens of applicants. Many of our most successful 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. Photographs and brief biographies of the current Resident & Fellow Section editorial team may be found in this Highlights booklet.

Over the years, the RFS has also introduced several subsections, which focus on (1) clinical neurologic education, such as Clinical Reasoning; Pearls & Oy-sters, Child Neurology, and Teaching NeuroImages (including both static images and videos); (2) graduate medical training, such as International Issues and Education Research and Initiatives; and (3) career issues, such as Emerging Subspecialties in Neurology. In addition, a Right Brain section includes creative writing, Mystery Cases engage readers in interactive discussion of critical aspects of clinical neurology, and Media and Book Reviews provide valuable analyses of textbooks, eBooks, Apps, and other resources for neurologists. Descriptions of these subsections appear before each sample article in this Highlight booklet.

Other unique projects developed during the past decade include podcasts (beginning in 2007), weekly EPearls (2008), an annual Writing Award (first given in 2009), our website (launched in 2010), the Journal Club (2011). 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 January 2012. In 2012, we also began making all Teaching NeuroImages available as teaching slides. In 2014, we completed our first research project, initiated by editorial team members, to explore the role of journal article mentored peer review as a way of teaching evidence-based medicine to residents. The project, funded through an American Academy of Neurology education research grant, involved residents at nine residency programs throughout the country, 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 is a brand new section of NCP that aims to identify and discuss difficult clinical scenarios and diseases with conflicting or insufficient evidence regarding diagnosis or treatment.

Last year’s recognition of the accomplishments of the first decade of the RFS were accompanied by change and visions for the future. Dr. John Millichap, a former editorial team member and the new RFS associate editor, assumed leadership of the section from Dr. Elkind as of July 1, 2015. He is joined by Deputy Associate Editor Roy Strowd, another former editorial team member. Their future endeavors will be limited only by the imagination and efforts of team members and others interested in neurology education. Plans are already in motion for several projects. First, the RFS will publish a Clinical Reasoning book of previously published cases complied to provide an educational resource for trainees and program directors. After that, we hope to engage new residents with a RFS welcome program of resources and information about the section. Other projects in development include “Journal Editing 101,” a formal three-year curriculum for the editorial team members, a mentor-mentee program designed to pilot new methods for guiding the transition of residents and fellows from authors to high-quality peer reviewers, and an update to the RFS website with new opportunities for a blog. 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.

The RFS has been 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, Sandi Moriarity, and Robert Witherow 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 kpieper@neurology.org. We hope you enjoy this year’s edition of the Highlights of the RFS!

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

Sara Stern-Nezer, John J. Millichap, Roy E. Strowd

Visit the Resident & Fellow Section (RFS) website at Neurology.org/site/feature/index.xhtml to access the features below.

1. The Clinical Reasoning subsection presents challenging cases and has sections with questions for consideration that help develop critical thinking skills in neurology. It can be the basis for an educational conference, a morning report case, or is a great starting point for incoming residents to hone their neurologic skills.

2. Each Teaching *NeuroImage* has a supplemental PowerPoint slide set available for download from the *Neurology* website that may be used for group presentations or a rapid review of illustrative or unique imaging findings.

3. 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.

4. The Emerging Subspecialties in *Neurology* subsection can provide valuable new ideas and viewpoints for residents considering different career options. The RFS website provides a link to the AAN Fellowship Directory.

5. The Media and Book Reviews section evaluates written and Electronic resources for residents, assisting them with finding the best resources to complement their training. In addition to traditional texts, the RFS reviews neurology apps and other electronic media. This is also a great way for residents to review new books or electronic media which as a reviewer they will get for free!

6. The Right Brain subsection allows residents to exercise their “write” brain by composing narratives, poems, or other expressions of their experiences as clinicians.

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

8. 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.

9. Follow the RFS on Facebook: Join our group entitled ‘American Academy of Neurology Residents and Fellows.’ For further digital access to RFS content, download the *Neurology* app onto your iPad®, listen to the weekly *Neurology* podcast which includes the E-Pearl of the week, and follow *Neurology* Twitter for updates.

10. Help to spread the word! Encourage your trainees to read the RFS regularly and send us manuscript submissions!
Announcement

*Neurology* Resident & Fellow Section Writing Award

The winners of the 2016 Award are:

**Sunil A. Mutgi MD, Alicia M. Zha MD, and Reza Behrouz DO,** for their article:  
Emerging Subspecialties in Neurology: Telestroke and teleneurology

The winners will be honored at the 2016 AAN Awards Luncheon. See page 22 of this Highlights.

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 2017 and will be awarded for a paper published in 2016.

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

**PAST RECIPIENTS**

**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
E-Pearls of the Week

June 8, 2015: Ondine’s Curse

Ondine’s curse, or congenital central hypoventilation syndrome (CCHS) is a rare neurologic based respiratory disorder, with an incidence of 1 per 200,000 live births\(^1\). First described in 1962 by Severinghaus and Mitchell, CCHS results in alveolar hypoventilation in sleep, most prominent during slow-wave sleep and rarely in wakefulness\(^2\). Treatment requires mechanical ventilator support, often lifelong. A large series found an association with Hirschprung disease and found mutations in the PHOX2B gene in 91\% of cases\(^1\). PHOX2B is a homeobox gene implicated in the development of the autonomic nervous system.

References


Submitted by Adam Numis, MD, Department of Neurology, University of California, Los Angeles

August 17, 2015: “Nav”igating painful neuropathies

Neuropathic pain is a common reason for referrals to neurology clinics. There is increasing evidence to support involvement of sodium channels in painful, small-fiber, neuropathies. Small-fiber neuropathies affect the myelinated A-fibers and unmyelinated C-fibers, resulting in pain and associated autonomic features. The voltage-gated sodium channels, Nav1.7 to 1.9, are preferentially found in the peripheral nervous system and are involved with the generation and propagation of action potentials in the nociceptive pathways. These channels, encoded by the SCN9A, SCN10A and SCN11A genes, are expressed within the dorsal root and autonomic ganglia. Mutations in these genes often lead to gain-of-function and increased firing rates or lowered thresholds within the dorsal root ganglion. Mutations in the Nav1.7 channel are associated with inherited erythromelalgia, characterized by recurrent attacks of symmetric intense pain, erythema, warmth, and swelling of the feet. Further expansion of the understanding of sodium channelopathies and their association with small-fiber neuropathies will help lead to better treatment options.

References


Submitted by James Addington, MD, Resident Physician, Department of Neurology, University of Virginia
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.
Child Neurology: Andersen-Tawil syndrome

Andersen-Tawil syndrome (ATS) is one of the periodic paralyses. This autosomal dominant disorder was initially named after Andersen, who in 1971 reported the case of a young boy presenting with intermittent muscle weakness, ventricular arrhythmias, and other developmental abnormalities. It was subsequently renamed Andersen-Tawil syndrome following the additional work of Dr. Rabi Tawil. Periodic paralysis, cardiac arrhythmias, and dysmorphic features are now recognized as the 3 characteristic features in patients with ATS.1, 2

CLINICAL CASE The proband is a 14-year-old boy who presented at the age of 9 years with recurrent episodes of leg weakness lasting several days. These episodes became more frequent, occurring at least once a month. The severity of the weakness during the episodes varied from mild weakness to inability to walk unassisted (2-3/5 weakness of proximal leg muscles). There were no clear triggers. Serum potassium levels measured during episodes of weakness were normal. Neurologic examination between episodes demonstrated proximal weakness (4/5) in the lower and upper extremities and a positive Gower sign. Treatment with potassium supplementation and acetazolamide resulted in mild clinical improvement. Family history revealed that his mother had had similar episodes that began during adolescence, improved with age, and resolved in her 40s. Potassium levels were reported to be low during her acute episodes. Sequencing of CACN1AS and SCN4A in the proband did not reveal any abnormalities. Several years after presentation, the proband’s 14-year-old brother developed a ventricular tachycardia. He had no history of weakness and his neurologic examination was normal. The combination of periodic paralysis and family history of cardiac arrhythmia prompted the testing of KCNJ2 for ATS. A pathogenic heterozygous missense c.652C>T (p.R216W) mutation was identified that segregated with the phenotype in the family. In retrospect, the proband, his brother, and his mother were noted to have mild dysmorphic features (micrognathia [figure], clinodactyly of the 5th fingers of the hands, and syndactyly of the 2nd and 3rd digits of the left foot). ECG and cardiac Holter monitoring of the proband did not reveal any abnormalities.

DISCUSSION Clinical features. ATS is one of the first known channelopathies; causal mutations have been identified in KCNJ2 on chromosome 17q24, which encodes the inward rectifier potassium channel 2 protein, Kir2.1.3 The dominant mutations in the Kir2.1 channel have a dominant negative effect on the potassium current (i.e., the mutated protein loses its normal function and adversely affects the function of the normal protein), resulting in prolonged depolarization of the action potential, thereby accounting for the cardiac and muscular symptoms.4 Autosomal recessive mutations in Kir2.1 have also been reported.4 Recently, a mutation in KCNJ5, which encodes the Kir3.4 subunit, has been linked to ATS and is thought to exert an inhibitory effect on the inward rectifier potassium current.5

In ATS, episodes of periodic paralysis first develop during childhood or adolescence and typically last between several hours and several days. Serum potassium levels during the episodes may be normal, elevated, or reduced. Although most cases seem to be associated with hypokalemia, several recent studies suggest normal potassium levels in patients with ATS.1, 6 Triggers of the paralytic episodes mainly include prolonged exercise, prolonged rest, rest after exercise, and emotional stress. Patients usually present with mild permanent proximal weakness.

Cardiac manifestations include ventricular arrhythmias as well as electrocardiogram abnormalities such as long QT interval, pronounced U waves, and long QTU interval.2 Patients may develop fainting spells or, in some cases, present with cardiac arrest leading to sudden death. ATS is also classified as “long QT syndrome type 7” (LQTS7), although the QT interval is either normal or only slightly prolonged in most cases.7

From the Division of Pediatric Neurology (M.A., M.S.), Montreal Children’s Hospital-McGill University Health Center, Montreal, Canada; and Division of Pediatric Neurology (M.A.), King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

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.
In addition to skeletal and cardiac muscle abnormalities, patients with ATS have dysmorphic features that are usually subtle. In fact, the use of the term “distinctive facial features” may be more appropriate. Dysmorphisms include broad forehead, hypoplastic mandible, hypotelorism, short palpebral fissures, short nose with fullness along the bridge and bulbous tip, thin upper lip, high arched or cleft palate, triangular facies, digit clinodactyly, syndactyly of the 2nd and 3rd toes, and short stature.

Patients with ATS have a distinct neurocognitive phenotype characterized by deficits in executive function and abstract reasoning.

ATS is a syndrome with a very high degree of phenotypic variability and is therefore very difficult to diagnose. The characteristic triad of clinical features (ventricular arrhythmias, periodic paralysis, and dysmorphic features) is present in 58%–78% of patients with KCNJ2 mutations, whereas between 32% and 81% present with involvement of only 2 of the 3 organ systems. Approximately 60% of the patients with a clinical diagnosis of ATS have causal mutations identified in KCNJ2. About 6%–20% of mutation-positive individuals do not exhibit any of the associated features, indicating that this disorder has incomplete penetrance.

**Differential diagnosis.** The diagnosis of ATS should be considered in any individual who displays at least 2 of the characteristic triad of symptoms, i.e., periodic paralysis, cardiac abnormalities, and facial dysmorphism. The differential diagnosis of ATS includes other periodic paralyses, namely hypokalemic periodic paralysis, hyperkalemic periodic paralysis, and thyrotoxic periodic paralysis.

The onset, duration, and severity of attacks in patients with hypokalemic or hyperkalemic paralysis are similar to those in ATS. Hypokalemic paralysis is associated with low serum potassium levels, whereas patients with hyperkalemic periodic paralysis generally have increased levels of serum potassium. In patients with ATS, periodic paralysis can occur with normokalemia, hyperkalemia, or hypokalemia. Nevertheless, the absence of the other typical features present in ATS (cardiac abnormalities and mild dysmorphic features) generally distinguishes patients with both hyperkalemia and hypokalemia from those with ATS. The presence of myotonia is characteristic of hyperkalemic periodic paralysis, and a majority of the patients with hypokalemic paralysis have mutations in the CACNA1S or SCN4A genes.

**Management.** Treatment strategies for ATS are generally directed toward the management of the periodic paralysis and cardiac arrhythmias. A thorough examination involving blood chemistry, including serum potassium concentration and thyroid function, should be done at baseline and during attacks. Cardiac evaluation including ECG and Holter monitoring should be performed, and patients should be followed by a cardiologist. Characteristic abnormalities of the heart, including prominent U waves, prolonged Q-U intervals, premature ventricular contractions, and bidirectional ventricular tachycardia, may be noted on ECG. Similarly, the use of 24-hour Holter monitoring will aid in examining the presence, frequency, and duration of ventricular tachycardia. Carbonic anhydrase inhibitors (such as acetazolamide 250–1,500 mg/day and dichlorphenamide 50–200 mg/day) have been used to reduce recurrent attacks of paralysis. Daily potassium supplements may be used in cases in which attacks are associated with hypokalemia. This can be an attractive option since elevated potassium levels shorten the QTc interval and decrease cardiac arrhythmogeneity. Cardiac pacemaker or defibrillators may be required in some patients.

Analysis of mutations in KCNJ2 is the only confirmatory genetic test so far. Genetic counseling, including thorough screening of family history, must be conducted, as it enables early treatment and prevention, especially of cardiac complications.

**CONCLUSION** ATS should be considered in the differential diagnosis of patients with periodic paralysis. The clinical triad of ATS consists of periodic paralysis, cardiac arrhythmias, and dysmorphic features. However, due to its phenotypic heterogeneity and subtle physical findings, ATS can be difficult to diagnose. Because some of the cardiac manifestations...
of ATS can be dangerous and life-threatening, establishing the accurate diagnosis of ATS is critical.

AUTHOR CONTRIBUTIONS
Mohammed Almuqbil drafted and revisied the manuscript for intellectual content. Myriam Srour drafted and revised the manuscript for intellectual content.

ACKNOWLEDGMENT
The authors would like to thank the patient and his family for their valuable participation.

STUDY FUNDING
No targeted funding reported.

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

REFERENCES
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:
A 56-year-old man with cognitive impairment and difficulty tying his necktie

SECTION 1
A 56-year-old previously healthy man presented with cognitive complaints. He described forgetting recent conversations and leaving tasks unfinished. He reported no problems with long-term memory, no personality changes, and he continued to perform all activities of daily living (ADLs) independently. His initial neurologic examination was normal, including a perfect score on the Mini-Mental State Examination (MMSE). Over the next 2 years, he developed difficulty reading his analog watch, managing finances, and making simple calculations while shopping. He also reported difficulty tying his necktie.

Questions for consideration:
1. What is the differential diagnosis for the patient’s cognitive decline?
2. What features on examination could help narrow the differential diagnosis?
SECTION 2
Cognitive decline more than expected for age with preserved independent ADLs suggests mild cognitive impairment, which progresses to dementia at an annual rate of 5%–15%. In addition to Alzheimer disease (AD), the differential diagnosis for our patient’s subsequent cognitive decline includes vascular dementia, dementia with Lewy bodies (DLB), and frontotemporal lobar degeneration (FTLD). Potentially reversible etiologies such as metabolic (vitamin B\textsubscript{12} deficiency), endocrine (hypothyroidism), toxic syndromes (medication effects), structural lesions (primary or metastatic brain tumor), and psychiatric conditions (depression) must be excluded as well. The patient’s B\textsubscript{12} and thyroid-stimulating hormone levels were normal. His complaints of difficulty tying his necktie could be due to deficits in strength, coordination, sensation, or higher-level action sequencing, requiring further characterization.

On neurologic examination, the patient scored 26/30 on the MMSE (figure, A). Formal neuropsychiatric testing confirmed deficits in multiple cognitive domains including memory, executive function, attention, and visuospatial skills with relative preservation of language. Strength, sensation, and reflexes were normal, without tremor or ataxia. He had increased tone, cogwheeling, and slowed finger tapping in the left arm, but normal right arm tone and movements. When attempting to pantomime use of a saw with his left hand, his hand moved in a circular motion. When asked to mimic waving goodbye with his left hand, he simply held his hand parallel to the table. Right-handed gestures were normal. Similarly, he had interval progression of his motor symptoms and now had masked facies, decreased blink rate, and decreased arm swing on the left when walking, though there was no retropulsion.

Questions for consideration:
1. How do the patient’s examination findings thus far contribute to determining the differential diagnosis?
2. Which additional features on history and examination could help narrow the differential diagnosis?

(A) The patient was asked to copy the overlapping pentagons, demonstrating marked difficulty with visuospatial constructions. (B) Axial fluid-attenuated inversion recovery MRI shows right greater than left parietal and frontal atrophy, out of proportion to age. (C) FDG-PET shows right greater than left hypometabolism in the basal ganglia, temporal lobes, and parietal lobes.
SECTION 3
The patient’s examination demonstrates asymmetric parkinsonism, but no resting tremor or shuffling gait. The patient’s difficulty with motor tasks in the setting of preserved strength, sensation, and coordination suggests apraxia. His inability to pantomime to verbal command and difficulty imitating gestures are consistent with ideomotor apraxia. Difficulty tying his necktie was possibly due to both difficulty sequencing the component actions (ideational apraxia) and diminished dexterity (limb-kinetic apraxia).

The differential diagnosis for parkinsonism with cognitive decline includes idiopathic Parkinson disease (PD) with PD-associated dementia, DLB, progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and multiple system atrophy (MSA). Parkinsonism typically precedes dementia in PD-associated dementia, while dementia may precede parkinsonism in DLB.

SECTION 4
This combination of asymmetric parkinsonism and cortical sensory deficits is characteristic of corticobasal syndrome (CBS). Although this patient has prominent asymmetric parkinsonism on examination, he lacks other features of synucleinopathies, such as anosmia, constipation, and REM sleep disorder. The presence of early cognitive features is atypical for PD, and there were no hallucinations or fluctuations to suggest DLB. He had no symptoms of autonomic or cerebellar dysfunction to suggest MSA, and no early features of PSP such as postural instability or falls. The characteristic vertical gaze impairment of PSP is usually a late finding, so its absence does not exclude this diagnosis.

CBS is characterized by asymmetric parkinsonism and cortical deficits. Diagnostic criteria differentiate between probable and possible CBS. Probable CBS requires the asymmetric presentation of at least 2 of the following features: limb rigidity or akinesia, dystonia, or myoclonus; and least 2 of the following: orobuccal or limb apraxia, cortical sensory deficit, or alien limb phenomenon. Possible CBS is suggested by the symmetric presentation of probable CBS features, but requires only one feature from each category.2 Our patient met criteria for probable CBS with asymmetric rigidity, dystonia, myoclonus, apraxia, cortical sensory deficits, and the alien limb phenomenon. CBS describes a clinical syndrome, while CBD is a pathologic diagnosis. CBS may be caused pathologically by CBD, AD, PSP, or FTLD. Our patient underwent MRI and FDG PET, shown in the figure.

Question for consideration:
1. How do these additional history and examination findings narrow the differential diagnosis?

SECTION 5
MRI demonstrated global atrophy disproportionately affecting the right parietal lobe including the postcentral gyrus (figure, B). PET revealed decreased tracer uptake in the right basal ganglia and bilateral parietal lobes, right more than left (figure, C). Focal asymmetric parietal and basal ganglia atrophy3 and hypometabolism4 are consistent with CBS.

Question for consideration:
1. How is CBS treated?
Although there is no disease-modifying treatment for CBS, many symptoms can be controlled pharmacologically. Levodopa may be used for parkinsonism but is often unsuccessful. Dystonia may respond to botulinum toxin injection; myoclonus can be treated with benzodiazepines or levetiracetam.

Cognitive symptoms may respond to acetylcholinesterase inhibitors and NMDA receptor antagonists, particularly if the underlying cause is AD pathology, but may worsen behavioral symptoms in patients with underlying FTLD pathology. Nonpharmacologic interventions include physical and speech therapy, and patients should be routinely assessed for the development of dysphagia.

Our patient was treated with levodopa, with minimal effect on his parkinsonism. His intermittent dystonia and myoclonus did not interfere with his daily functioning and therefore did not require specific intervention. Physical therapy and speech therapy allowed him to ambulate with assistance and tolerate a regular diet. His cognitive symptoms progressed clinically to dementia, requiring assistance on most of his ADLs, although he continues to live at home with aid from his family.

**DISCUSSION** CBS can be caused pathologically by multiple entities. When characteristic tau-positive lesions are found on autopsy, the condition is referred to as CBD. In autopsy series, CBD, AD, and PSP all account for about 25% of cases. The remainder is composed of pathology consistent with FTLD or PD.

Although CBD, PSP, and AD are all tauopathies, they differ in the specific tau isoform involved (4R in CBD and PSP vs 4R and 3R in AD), as well as gross and microscopic findings at autopsy. In CBD, histology demonstrates ballooned cortical neurons, tau-positive astrocytic plaques, and tau-positive thread-like lesions in the neuropil of gray and white matter throughout the cortex and basal ganglia. The characteristic lesion of PSP, the tufted astrocyte, is found in a similar distribution, though typically with less cortical involvement than in CBD. Additionally, prominent midbrain atrophy differentiates PSP from CBD. The hallmark of AD pathology is amyloid-containing senile plaques and involvement of the hippocampi. Many cases of CBS have mixed underlying pathology.

Clinical criteria have been proposed to distinguish patients with CBD from other pathologic causes of CBS. Probable sporadic CBD requires probable CBS beginning at or after age 50 years, excluding patients with positive family histories or suspected tau-related genetic mutations. Possible CBD is characterized by insidious onset and gradual progression of possible CBS over at least 1 year. The accuracy of these criteria ranges from 47% to 68%. Our patient meets criteria for probable CBD as the underlying etiology based on age and no family history of similar disorders.

As specific therapies for AD and other tau-associated diseases emerge, antemortem clinical and radiologic predictors of underlying pathology in patients with CBS are essential. Early memory loss and early visuospatial deficits, both present in our patient, may predict underlying AD pathology. Quantitative MRI using voxel-based morphometry can identify relatively focal patterns of atrophy in specific areas of the posterior frontal lobes in CBD compared to more widespread atrophy when AD is the underlying etiology of CBS. When consistent with AD, Pittsburgh compound B–PET imaging and CSF biomarker profiles can serve as additional exclusion criteria for possible and probable CBD. Continued advances in biomarkers offer the possibility for earlier differentiation of underlying pathologic subtypes of CBS, and potentially earlier trials of disease-modifying agents.

**REFERENCES**


General Submission Instructions

The Resident & Fellow Section is a primarily online feature that serves the resident and fellow readership. Residents and fellows are expected to be the primary authors for most submissions, but those highly involved in graduate medical education (e.g., program directors) may also contribute submissions on appropriate topics. Submissions for all article categories should be no more than 1,500 words; permission for longer articles will be needed from the editors. The number of references should be 10 or less and one to two tables or figures may be incorporated. The topic must be mentioned in the cover letter of the submission. Potential article topics include: Teaching, ethics, practice, career choices, residency training, editorial, international education, research, historical, opinion, book review, training videos, or teaching NeuroImages. Teaching NeuroImages has the same requirements as NeuroImages but is especially valuable to the trainee audience and will be published in the online Resident & Fellow Section. Queries and comments should be addressed to Kathy Pieper at kpieper@neurology.org.
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*. 
ABSTRACT

Background: In 2012, the American Academy of Neurology (AAN) updated and expanded its ethics curriculum into Practical Ethics in Clinical Neurology, a case-based ethics curriculum for neurologists.

Methods: We piloted a case-based bioethics curriculum for neurology residents using the framework and topics recommended by the AAN, matched to clinical cases drawn from Columbia’s neurologic services. Our primary outcome was residents’ ability to analyze and manage ethically complex cases as measured on precurriculum and postcurriculum multiple-choice quizzes. Secondary outcomes included precurriculum and postcurriculum self-assessed comfort in discussing and managing ethically complex cases, as well as attendance at ethics discussion sessions as compared to attendance at other didactic sessions.

Results: Resident performance on quizzes improved from 75.8% to 86.7% (p = 0.02). Comfort in discussing ethically complex cases improved from 6.4 to 7.4 on a 10-point scale (p = 0.03). Comfort in managing such cases trended toward improvement but did not reach statistical significance. Attendance was significantly better at ethics discussions (73.5%) than at other didactic sessions (61.7%, p = 0.04).

Conclusion: Our formal case-based ethics curriculum for neurology residents, based on core topics drawn from the AAN’s published curricula, was successfully piloted. Our study showed a statistically significant improvement in residents’ ability to analyze and manage ethically complex cases as measured by multiple-choice tests and self-assessments.

GLOSSARY

AAN = American Academy of Neurology; ACGME = Accreditation Council for Graduate Medical Education.

Clinicians and medical educators from numerous specialties including neurology have noted an increasing quantity and complexity of bioethical dilemmas and have advocated formal ethical training as part of all residency curricula. The goal of this training is twofold:

1. To supply the knowledge and cognitive skills necessary for analyzing and making ethical decisions in complex clinical environments
2. To promote the specific attitudes and values deemed necessary to the moral development of the health care professional—a process of “professionalization” or “moral enculturation”

In 1996, the Accreditation Council for Graduate Medical Education (ACGME) mandated that every residency curriculum must include ethics education, for the specific purpose of promoting the ACGME core competency of Professionalism.

In 2000, the American Academy of Neurology’s (AAN’s) Ethics, Law, and Humanities Committee published the first pilot ethics curriculum specifically designed for neurology residents. One study showed this older curriculum to be effective in improving residents’ knowledge of bioethics. In 2012, the AAN updated and expanded this pilot curriculum into Practical Ethics in Clinical Neurology: a case-based ethics curriculum for residents, fellows, and practicing neurologists. This is the curriculum currently recommended by the AAN for compliance with the ACGME’s requirement for ethics education in residency.

Prior to July 2011, the Columbia University neurology residency program lacked a formal ethics curriculum. Our objective therefore was to demonstrate that a formal case-based bioethics curriculum, specifically
employing the current topics and framework laid out by the AAN, could improve residents’ ability and self-assessed comfort in discussing and managing ethically complex cases. Our hypothesis was that residents’ skill and comfort would improve over the course of the curriculum.

METHODS Study population. The study involved all 31 residents in Columbia University Medical Center’s neurology department. Of these, 24 residents completed precurriculum and postcurriculum quizzes and surveys, with 7 others not completing both evaluations.

Intervention. The authors first created a list of key topics from the AAN’s 2000 and expanded 2012 ethics curricula, focusing on those topics that residents found most challenging and with which they most frequently grappled.6,8 Topics were drawn from the overarching categories of professionalism, clinical decision-making, death and dying, and special topics in neuroethics. These topics were then matched to cases from Columbia University’s inpatient and outpatient neurologic services. This was in keeping with the recommendation of many medical educators and ethicists, who assert that trainees are most actively engaged in case-based discussions, and particularly when these involve real cases in which the trainees have actually participated.1 For example, the case of an elderly woman newly diagnosed with glioblastoma multiforme, whose family asked that she not be informed of the diagnosis, was used to address the issues of confidentiality and truth-telling (key topics within the domain of professionalism). The case of a man with amyotrophic lateral sclerosis who publically announced his intention to commit suicide rather than accept tracheotomy was used to discuss the topics of advanced directives (a key topic related to clinical decision-making), physician-assisted suicide, and palliative care (key topics related to death and dying).

The curriculum began with simulation sessions utilizing professional actors provided by Columbia University Medical Center’s Simulation Center. All postgraduate year 2 residents completed a short didactic session on the 6-step protocol setting, perception, invitation, knowledge, emotions, summary (SPIKES) for delivering bad news to patients.9 The residents then each practiced delivering a poor diagnosis to a simulated patient/actor in an ethically complex situation (e.g., delivering news of likely brain death to a family that does not accept brain death for religious reasons). They then watched their coresidents providing poor diagnoses, and engaged in mutual feedback with the guidance of senior simulation center and neurology department attendings.

Following the introductory simulation sessions, all bioethics discussions occurred during mandatory 1 hour noon conferences and were generally formatted along the following guidelines: a resident or attending would briefly present a clinical case; whenever possible, one that he or she had actually managed. The case presentation would then be followed by a discussion facilitated by at least 2 discussion leaders. These discussion leaders were senior attending physicians including at least one neurologist and at least one member of the hospital ethics committee. The ethics committee members were typically not neurologists, and were able to offer insights from specialties such as critical care medicine, internal medicine, psychiatry, and palliative care. The authors met with the discussion leaders and presenting residents before each case discussion to determine which specific topics would be addressed in connection with the presented case.

RESULTS Over the course of the first 9 months of the year, we ran 1 simulation session and 12 bioethics case discussions. Each case was matched to ethics topics drawn from the AAN’s Practical Ethics in Clinical Neurology curriculum.

Primary outcome. Residents averaged 75.8% on the precurriculum quiz on the management of ethically complex cases, and improved to an average of 86.7% on the postcurriculum quiz (p = 0.02). Each class of residents (postgraduate years 2, 3, and 4) improved their quiz performance (table).

Secondary outcomes. Self-assessed resident comfort in discussing ethically complex cases increased from a mean of 6.4 on a 10-point scale precurriculum to a mean of 7.4 postcurriculum (p = 0.03). Self-assessed resident comfort in managing ethically complex cases trended toward improvement from an average of 6.5 on a 10-point scale precurriculum to an average of 7.0 postcurriculum (p = 0.07).

The average attendance for ethics discussions was 73.5%, as compared to 61.7% for noon conferences on the days preceding ethics discussions (p = 0.04).

DISCUSSION This study formally examines the effects of implementing the AAN’s recently published bioethics curriculum for neurologists. It showed an improvement in residents’ ability to analyze ethically complex cases on precurriculum and postcurriculum multiple-choice tests. The study also showed an improvement in residents’ self-assessed comfort in
Table Precurriculum and postcurriculum quiz and self-assessment results

<table>
<thead>
<tr>
<th></th>
<th>Precurriculum</th>
<th>Postcurriculum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Postgraduate year 2 (n = 7)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quiz scores, %</td>
<td>82.9</td>
<td>88.6</td>
</tr>
<tr>
<td>Comfort managing cases</td>
<td>6.57</td>
<td>7.14</td>
</tr>
<tr>
<td>Comfort discussing cases</td>
<td>5.29</td>
<td>7.43</td>
</tr>
<tr>
<td><strong>Postgraduate year 3 (n = 9)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quiz scores, %</td>
<td>64.4</td>
<td>77.8</td>
</tr>
<tr>
<td>Comfort managing cases</td>
<td>6.22</td>
<td>7.33</td>
</tr>
<tr>
<td>Comfort discussing cases</td>
<td>7.11</td>
<td>7.56</td>
</tr>
<tr>
<td><strong>Postgraduate year 4 (n = 8)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quiz scores, %</td>
<td>82.5</td>
<td>95.0</td>
</tr>
<tr>
<td>Comfort managing cases</td>
<td>6.63</td>
<td>6.63</td>
</tr>
<tr>
<td>Comfort discussing cases</td>
<td>6.63</td>
<td>7.13</td>
</tr>
<tr>
<td><strong>Total (n = 24)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quiz scores, %</td>
<td>75.8</td>
<td>86.7</td>
</tr>
<tr>
<td>Comfort managing cases</td>
<td>6.46</td>
<td>7.04</td>
</tr>
<tr>
<td>Comfort discussing cases</td>
<td>6.42</td>
<td>7.38</td>
</tr>
</tbody>
</table>

Future directions. This study provides a basis for a randomized controlled trial of the AAN’s ethics curriculum, to determine whether our observed benefits are the result of the formal curriculum rather than ordinary clinical experience. These studies would ideally be performed across multiple training programs to assure generalizability of the results. Because our current results suggest that more attention is needed to manage ethically complex cases, we plan to incorporate into the curriculum 3 or 4 additional case simulations focusing on family discussions regarding goals of care, life support, and patients’ religious and cultural values. These simulations and the case discussions should be aligned with specific educational milestones in keeping with the latest recommendations of the Outcome Project of the ACGME and the American Board of Medical Specialties.  

AUTHOR CONTRIBUTIONS

Benjamin Tokchin: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, acquisition of data, statistical analysis.

Joshua Z. Willey: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, study supervision. Kenneth Prager: drafting/revising the manuscript, study concept or design, accepts responsibility for conduct of research and final approval.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

B. Tolchin reports no disclosures relevant to the manuscript. J. Willey receives K23 funding from the NIH/National Institute of Neurological Disorders and Stroke for an unrelated project and reports no other disclosures. K. Prager reports no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES

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: Telestroke and teleneurology

In 2013, Dall et al.¹ projected that by 2025, the societal need for neurologists will exceed availability by 19%. This number failed to account for the disproportionate number of neurologists practicing in urban and academic centers, likely underestimating the gap in rural populations. In a recent effort to improve access to neurologic services in these areas, telestroke and teleneurology networks have been championed as the solution. With the emergence of these networks come unique challenges and opportunities in the distribution and breadth of neurologic care that fellows and residents will need to understand to optimally incorporate this tool into their future practices.

History and development. Telemedicine was first conceptualized in 1924 in Radio News Magazine, where the idea of a future including “video-radio” for medical diagnosis and management was introduced.² The American Telemedicine Association formally defines the term to mean the use of medical information exchanged from one site to another via electronic communications to improve a patient’s clinical health status. This concept continues to undergo extensive metamorphosis as technology has evolved and as implementation within multiple medical subspecialties has grown. In neurology, 2 terms are now used in general practice: teleneurology, the application of telemedicine to the field of neurology; and telestroke, a subdivision of teleneurology involving telemedicine consultation for the treatment of neurovascular patients. Both definitions are conventionally accepted within the field and are recognized to include the use of high-quality audio-video conferencing with or without the inclusion of electronic medical records, radiographic imaging, or other physiologic data.³-⁵

Initial rudimentary implementations of telemedicine consisted only of remote telephone consultations between physicians. In time, this tool has come to encompass remote audio-video consultations and electronic transmission of radiographic imaging with or without physiologic data and electronic medical records.³ Regrettably, for many years, barriers to implementation existed that limited application of telemedicine systems to grant-funded tertiary academic centers and widespread acceptance of telemedicine was nonexistent.³,⁴,⁵ Initially, these barriers appeared insurmountable—video systems were bulky, software was insecure, high-speed network access was scarce, physical examinations were not standardized, credentialing responsibilities were unclear, and reimbursement for services was undefined.³-⁶ Despite these and other barriers to widespread implementation, the tide did eventually turn following the results of the National Institute of Neurological Disorders and Stroke recombinant tissue plasminogen activator (rtPA) trial in 1996. With a Food and Drug Administration–approved time-sensitive treatment for stroke, the question of improving time to administration was forefront. In 1999, Levine and Gorman⁷ provided the answer, in their landmark article “‘Telestroke’: the application of telemedicine for stroke,” in which they demonstrated that rtPA could be safely administered remotely by telemedicine.

With physicians finally able to justify the high cost of advanced telemedicine implementation and utilization, telestroke progressively became more widespread and other barriers slowly began to dissolve. To improve diagnostic accuracy, remote physical examination of suspected stroke patients has become standardized. The NIH Stroke Scale (NIHSS), now a well-established and validated assessment, was developed and implemented.⁷ Technology has continued to evolve under pressure for more portable communication systems and telemedicine consultations can now be provided from anywhere if a laptop and high-speed Internet access are available. Billing and licensure concerns, while still valid, are being actively addressed at federal and local levels. Centers for Medicare and Medicaid Services have published rules allowing reciprocity of physician privileging and Medicare has improved reimbursement for telestroke consultation with implementation of Diagnostic-Related Group 559.⁴,⁵

With the implementation of telestroke spreading rapidly in the United States, a prevailing model has emerged and is becoming the gold standard. This model, known as the hub and spoke model, is centered on the understanding that large tertiary medical

From the Department of Neurology, Wexner Medical Center, The Ohio State University, Columbus.

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.
centers, known as hub hospitals, have access to resources not available to smaller spoke hospitals, making telestroke consultation mutually financially beneficial.4,8 In this model, the tertiary medical center has a rotating call schedule with a large group of trained vascular neurologists to respond to the telestroke consultations.4,8 This provides spoke hospitals continuous access to specialty evaluation for acute stroke patients.4,8 In 2013, Switzer et al.8 reported a cost-benefit analysis of this model, which validated that a mutual financial benefit does exist, but only when a skilled specialist is able to differentiate the patients best indicated for hospital transfer. In another analysis of the evolving hub-spoke system, Silva et al.4 conducted a survey in 2012 of multiple telestroke network sites and concluded that telestroke is a “widespread and growing practice model,” but that variations of the models exist. In their review, they noted that a percentage of hub systems reported utilizing contract neurologists as a component of their vascular neurology pool and that nearly 50% of the reviewed programs incorporated isolated telephone consultations into their telestroke model.4 In all variations reviewed, it was apparent that a well-implemented hub and spoke model is an effective method of implementing telestroke.4

With the success of telestroke, recent focus has turned to applications in general neurology. Between 2013 and 2014, 2 of the most comprehensive tele-neurology assessments to date were published, creating thought-provoking considerations for future implementation of teleneurology. The study by Davis et al.9 evaluated 354 patients treated under the Veterans Health Administration. All patients in the study underwent initial on-site clinical evaluation and appropriate ancillary testing followed by off-site teleneurology follow-up. The authors determined that clinical management and patient satisfaction were not affected by this model of outpatient teleneurology assessment.9 The second study was a review completed by Wechsler et al.7 as part of an American Academy of Neurology (AAN)—established Telemedicine Work Group. As this was not a clinical trial, they were only able to suggest potential impediments and advantages to teleneurology implementation. Most barriers noted were similar to those previously seen with telestroke network development. A new consideration in the outpatient setting was the doctor–patient relationship; however, this has been addressed in the simultaneous Davis et al.9 study. The workgroup did raise multiple potential benefits to more generalized teleneurology implementation in addition to those previously recognized in telestroke networks. Reduced travel time, reduced cost for patients, and improved access to care for immobilized patients were considered significant potential benefits by the AAN group, and these benefits were seen in the study by Davis et al.9 as well as in subsequent published reviews.7,10 Additionally, the AAN group suggested potential benefits of improved clinical trial recruitment, and utilization of teleneurology for enhanced resident–fellow education, yet unrealized benefits of teleneurology.7

How to prepare our residents and fellows for the future. Neurology is evolving to incorporate telemedicine into daily practice. The success or failure of this integration will depend on the skills endowed upon our rising residents and fellows. The current training for remote management of neurologic conditions utilizing telemedicine systems is limited outside of select neurovascular fellowship programs. Dependent on the abilities of a remote site, examinations can be facilitated either by utilizing standardized assessment scales such as the NIHSS or through instruction of a certified nurse who can remotely complete a detailed neurologic assessment, acting as an extension of the examiner. Development of the skills required to remotely interpret these complex neurologic examinations requires experience, best initially obtained under supervision.

As teleneurology continues to be incorporated into practice, it will need to also be integrated to a greater degree into the daily lives of trainees. Figure e-1 on the Neurology® Web site at Neurology.org notes general applications for inpatient and outpatient teleneurology. On the inpatient side, an expansion of consult services will likely occur to encompass the additional consultations generated from local hospitals through teleneurology, while transferred patients will continue to be integrated into existing hospital inpatient services. For outpatient services, the neurology community will likely begin to see follow-up of appropriately chosen patients in rural communities through teleneurology satellite clinics, easing the typical patient burdens associated with the cost of transportation to tertiary care centers. With multiuser teleneurology software available after establishment of a primary network, trainees will be able to be integrated into this process, taking the role of primary physician under the physical or electronic guidance of a licensed attending physician.

After sufficient supervised training, the fellows and new residents can be introduced to higher levels of independence utilizing the teleneurology system congruent with their individual level of training. Fellows will likely become more independently involved with spoke hospital assessments both in teleneurology and telestroke and residents would be able to conduct limited teleneurology assessments in place of traditional phone assessments for patient questions or concerns. By such integrations, rising residents and fellows will
develop the necessary skills to optimize the benefits of
teleneurology as we move into a future of possibility
while educating them to provide fiscally responsible
care and improving patient access to neurologic
specialists.

AUTHOR CONTRIBUTIONS
Sunil A. Mungi: initial conception of manuscript direction, evaluation of
the literature, and completion of final manuscript through multiple revi-
sions. Alicia M. Zha: direct participation in the structuring, revision, and
production of the final manuscript. Reza Behrouz: primary attending/
mentoring physician, direct participation in structuring the manuscript,
review of multiple drafts and revisions, providing instruction for revi-
sions, and approval of final manuscript.

STUDY FUNDING
No targeted funding reported.

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

REFERENCES
1. Dall TM, Storm MV, Chakrabarti R, et al. Supply and
demand analysis of the current and future US neurology
2. Field MJ; Institute of Medicine (US) Committee on Eval-
uating Clinical Applications of Telemedicine. Evolution
and Current Applications of Telemedicine. Available at:
http://www.ncbi.nlm.nih.gov/books/NBK45445/. Ac-
cessed July 17, 2014.
3. Levine SR, Gorman M. “Telestroke”: the application of
States a survey of currently active stroke telemedicine pro-
5. Switzer JA, Levine SR, Hess DC. Telestroke 10 telestroke
years later: telestroke 2.0. Cerebrovasc Dis 2009;28:
323–330.
applications: report of the Telemedicine Work Group of
the American Academy of Neurology. Neurol 2013;80:
670–676.
8. Switzer JA, Demaerschalk BM, Xie J, Fan L, Villa KF,
Wu EQ. Cost-effectiveness of hub-and-telestroke spoke
telestroke networks for the management of acute ischemic
stroke from the hospitals’ perspectives. Circ Cardiovasc
9. Davis LE, Coleman J, Harnar J, King MK. Teleneurology:
successful delivery of chronic neurologic care to 354
patients living remotely in a rural state. Telemed J E
and neurology: what is possible? Neurol Sci 2013;34:
2263–2270.

Thank you R&F Team!
The RFS editors and editorial staff would like to thank the following team members
for their assistance in the compilation of this Highlights booklet: Jennifer Cialone,
Ilena George, and Jonathan Kleinman.
International Issues

More than 85 percent of the world’s population lives in low and middle income countries, where the burden of neurological disease is the largest. Relatively little is known, however, about patients and practitioners of neurology in most countries. This section aims to explore international issues in neurology education. We welcome manuscripts describing international educational exchanges, personal rotations and experiences in low and middle income countries, and work by neurology trainees from around the globe. Descriptions of notable differences in training between countries are of interest. Inclusion of practical information regarding how interested residents might get involved in international programs would also be of use.
International Issues: An international survey of young neurologists’ perceptions of future health care and neurology

Antonella Macerollo, MD
Kristizta Róna-Vörös, MD
Walter Struhal, MD
Xenia Kobeleva, MD
Johann Sellner, MD

The future occupations and interests of the medical profession have to be in some respects different from those of the past, and they have to be more various.1

Medicine continues to evolve in response to our greater understanding of disorders and the discovery of new therapies. As the 21st century begins, once again neurology finds itself in a pivotal evolutionary point of its eventful history. Breakthrough discoveries linked to molecular biology and genetic engineering have made personalized medicine foreseeable.2 Information technologies have paved the way for consultation of remote patients and have adapted to the educational demands of upcoming neurologists, patients, and caregivers. Moreover, there has been an increase in the percentage of women in the neurology workforce.3 Importantly, the voice of junior neurologists is increasingly recognized and incorporated in decision-making processes at the national and continental level.4

The spectrum of neurology has been ever changing and frontiers have to be regularly redefined. In some countries, subspecialties have been established to deal with different needs required by acute and chronic neurologic diseases.5 Demand and allocation of specialized doctors is likely to be defined by 3 interconnected developments: the aging population, the parallel rise in chronic disease, and the affordability of health care. Indeed, contemporary health care is barely managing to cover its costs and gaps in sufficient neurology service have become evident across Europe.6

There are limited data available on the current visions of neurologists for health care and neurology. It would be interesting to know whether the upcoming generation of neurologists is aware of global health care concerns. We aimed to garner ideas about current challenges and future development of health care among residents and junior neurologists from member states of the European Union and neighboring countries. We further assessed emerging constraints for clinical practice as well as perceptions for the development of neurology subdisciplines and core competences.

METHODS Details on the Methods are in appendix e-1 on the Neurology® Web site at Neurology.org. The questionnaire is provided in appendix e-2.

RESULTS Demographics. A total of 86 participants completed the survey, yielding a participation rate of 80%. There were 45 in residency training (median 4.6 years [interquartile range (IQR) 1–12] since graduation from medical school) and 41 board-certified neurologists (for a median of 5.5 years [IQR 1–15]). The participants originated from the European Union or the European Economic Area (EEA) (n = 49; countries: Bulgaria, Croatia, Denmark, Estonia, Germany, Greece, Hungary, Italy, Lithuania, Macedonia, Poland, Portugal, Romania, Slovenia, Spain, Turkey, United Kingdom) and Eastern Europe (n = 30; countries: Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Moldova, Russia, Serbia, Ukraine). A minor group consisted of delegates from Africa and the Middle East (n = 7; Egypt, Iraq, Nigeria, Tunisia). From each country, there were 1 to 4 participants, except for Romania (n = 10) and Russia (n = 14). The analysis of country of graduation and current workplace revealed that 95.2% had remained in their home country.

Current perception about health care and neurology. The analysis of the perception for the current status of health care revealed that the majority were content, as 11% were highly satisfied and 35% somewhat satisfied (figure, A). On the other range of the scale, 30% showed a level of discontent (somewhat, 27%; highly, 3%). There was a higher percentage of satisfied people among Africans/Middle Eastern and Eastern Europeans compared to European Union/EEA.

From the Sobell Department of Motor Neuroscience and Movement Disorders (A.M.); The National Hospital of Neurology and Neurosurgery, Institute of Neurology, University College London, UK; the Department of Neuroscience and Sense Organs (A.M.); Aldo Moro University of Bari, Italy; the Department of Neurology (K.R.-V.); Keckemér Hospital, Kecskemét, Hungary; the Department of Neurology (W.S.); Allgemeines Krankenhaus Luz, Austria; the Department of Neurology (K.K.); Medical School Hannover, Germany; the Department of Neurology (J.S.); Christian-Doppler-Klinik, Paracelsus Medical University, Salzburg, Austria; and the Department of Neurology (J.S.); Klinikum rechts der Isar, Technische Universität München, Germany.

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 current feeling of satisfaction specifically for neurology was again assessed on a 5-level ranking scale (figure, B). The percentage of satisfied participants was higher than ones who were dissatisfied (46% and 35%, respectively), whereas 22% were neutral. The colleagues most satisfied with neurology in the home country came from Africa and the Middle East (43%), followed by those from Eastern Europe (37%). In contrast, only 8% from European Union/EEA reported high satisfaction.
Level of optimism regarding the future of health care and neurology and reasons for skepticism for the future of medicine. An optimistic future of general health care was anticipated by 83%. When asked about the future of neurology, 80% responded that they were optimistic (figure, C). The analysis of the demographic cohorts revealed a higher percentage of optimistic feeling for neurology among Africans and Middle Easterners (86%). Lower optimism rates were present among participants from Eastern Europe and European Union/EEA (50% and 47%, respectively).

Regardless of the level of optimism, we analyzed potential factors related to demonizing factors for the future of medicine. Three main factors were identified as reasons for skepticism: the expectation of a declining income and increasing living costs, distrust in the government, and the assumption that the revenue of the insurance would not be able to cover the increasing health care costs (table e-1). Analyzing the 3 demographic groups, we found differences for the European Union vs Eastern Europe vs Africa/Middle East (table e-1) for one to expect a progressive worsening of the health system (European Union/EEA, 43%; Eastern Europe, 10%; Africa/Middle East, 0%). Moreover, there were differences towards increase of clinical workload and nonclinical workload, which were important reasons of skepticism for the European Union and Eastern Europe but not for Africa/Middle East (table e-1).

In 10 years, will you be working as a neurologist? Where? Seventy-six percent of respondents expect to practice as a neurologist in 10 years. This finding was homogenous among the 3 demographic groups (figure, D). Only 35% estimated to remain in the originating country in 10 years. There was a higher rate among Africans/Middle Easterners (57%; figure, E).

Emerging subspecialties for neurologists. Most frequently, aging and dementia (85%), cerebrovascular disorders (82%), cognitive neurology (74%), neurodegenerative disorders (73%), and multiple sclerosis (72%) were considered to gain relevance in the future. There were no differences in the 3 demographic groups (table e-2).

Key competences. Among the key competences gaining further relevance in the future were neuroimaging (85%), neurogenetics (84%), and laboratory examinations (80%). We did not find differences in the 3 demographic groups (table e-3).

DISCUSSION The data presented are an effort to unveil the current visions of residents and young neurologists about the future of health care and neurology. The main finding was common optimism about health care as well as neurology. This enthusiasm is confirmed by the predominant plans to practice as a neurologist in 10 years. Interestingly, cross-border mobility might be considered, which corroborates the current interests in international relocation. The interest to relocate was prevailing and an increment of insufficient provision for neurologic service in certain areas can be anticipated. Hence, national bodies need to be aware of this mindset and counteract by raising the attractiveness for remaining in less attractive regions and countries.

Overall, young neurologists share the concerns of insufficient income and fear the subsequent impaired quality of life. The latter is viewed central in career decisions for the current generation of neurologists.7 Bradley8 proposed a rise in the number of medical graduates entering neurology residency between 2000 and 2020. The estimation was supported by the explosion of knowledge in neuroscience and potential insights into previously unclear disorders.9 There were differences among the demographic cohorts. The level of optimism was particularly high in Africans/Middle Easterners.

Regardless of the level of optimism, we inquired for potential reasons leading to constraints. An expected worsening of the health system was more important for colleagues from the European Union/EEA (43%) compared to Eastern Europe (10%) and Africa/Middle East (0%). Furthermore, there were differences in the expected consequences of the clinical and nonclinical workload, which were important reasons for skepticism in the European Union and Eastern Europe but not in Africa/Middle East.

The results of our survey highlighted that the upcoming generation of neurologists are aware of challenges related to demographic trends. The perception of subspecialties that will gain further importance included dementia, cerebrovascular diseases, cognitive neurology, and neurodegenerative diseases. Other relevant fields were movement disorders, sleep disorders, and multiple sclerosis, where bench to bedside approaches have been able to change diagnosis and treatment of disease over recent decades. Gene-based therapies and stem cell technology are predicted to have rapid development to delay or repair the progression of brain degeneration disease, as well as deep brain stimulation devices to treat the most serious cases of movement disorders.8 The respondents of this survey did not indicate neuroinfectious diseases to gain importance in the future, although the WHO rates infectious diseases as major issue that will gain further importance within the next years.10 This may be related to the recent development in many European countries that other disciplines have taken over the care of patients with neuroinfections (e.g., internal medicine, critical care medicine).

We assume a couple of biases and limitations of this study. First, a selection bias is likely, as participants of this international neurology course were self-nominated and mainly originating from academic departments, and more updated on the progress and demands in the wide
spectrum of neurologic subspecialties. This recruitment bias may also support the tendency to consider relocation.

Our survey confirms neurology in the 21st century being a dynamic area of medicine, with constant advances and transitions.

Our data suggest that talented junior colleagues continue to be attracted to neurology and acknowledge ever-changing demands and upcoming challenges.

AUTHOR CONTRIBUTIONS
Antonella Macerollo: study concept and design, data acquisition and analysis, drafting of manuscript. Krisztina Róna-Vörös: study concept and design, data acquisition and analysis. Walter Struhal: study concept and design, data analysis, manuscript revision. Xenia Kobeleva: study concept and design, data acquisition and analysis. Johann Sellner: study concept and design, data acquisition and analysis, drafting of manuscript and revision.

STUDY FUNDING
No targeted funding reported.

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

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 Neurology.org/content/early/recent 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: Randomized phase III study of whole-brain radiotherapy for primary CNS lymphoma

Primary CNS lymphoma (PCNSL) is a rare aggressive variant of extranodal non-Hodgkin lymphoma (NHL) that involves the brain, leptomeninges, eyes, or spinal cord. PCNSL is primarily treated with systemic high-dose methotrexate. The role of combining chemotherapy with whole-brain radiation therapy (WBRT) has been debated as WBRT is linked to delayed neurotoxicity, especially in patients older than 60 years. In 1999, the German PCNSL group initiated the largest and only phase III trial to date evaluating whether the omission of WBRT compromises OS in immunocompetent patients with PCNSL. The initial report at a median follow-up of 31.8 months was published in 2010. The updated version at a median follow-up of 81.2 months was recently published in Neurology.

HYPOTHESIS AND DESIGN The study questioned whether a regimen of high-dose methotrexate (HDMTX) alone for treatment of PCNSL was noninferior to combining chemotherapy with WBRT. A noninferiority (NI) design was utilized. NI designs are undertaken when it is unethical to compare the experimental treatment to placebo or a no-treatment control (when effective treatment is available, HDMTX in this case), and for comparative effectiveness research where the new treatment is potentially less toxic (as in this case) or less costly than the standard treatment. Thus, NI design was an appropriate approach for this study.

METHODS Immunocompetent patients, 18 years or older, with primary CNS lymphoma, treated at 75 centers in Germany between 2000 and 2009, were included. Major exclusion criteria included HIV-positive serology, concomitant malignancy, and pregnancy. Patients were randomized to receive HDMTX with or without WBRT via block randomization, which ensures that equal numbers of participants are assigned to each group. Addition of Ifosfamide to HDMTX was a protocol amendment because of continuous observation that HDMTX alone might have been insufficient as first-line therapy for PCNSL. Patients who received HDMTX with a known response status were included in the intention-to-treat (ITT) analysis. Patients assigned to the WBRT group received WBRT for the most part, with the exceptions of patients with complete response (CR: defined as complete resolution of contrast-enhancing lesions on MRI or CT) who refused further treatment and patients without CR who received chemotherapy or no treatment instead. Patients assigned to the no WBRT group who had CR did not receive further treatment, and those without CR who actually received WBRT and those who did not (based on group assignment). As-treated analysis compared patients with CR (regardless of group assignment) who received WBRT to those who did not receive WBRT, and patients without CR (again, regardless of group assignments) who received WBRT to those who received HD-Ara-C (outcome referred to as progression-free survival [PFS] from last HDMTX). The primary outcome of a study is the outcome on which the study’s power calculation is based. This study looked at OS (primary outcome, measured from time of randomization until death) as well as PFS (secondary outcome, measured from time of randomization until first progression of disease). This study had 60% power to prove NI using a NI margin of 0.9. In other words, NI was to be concluded if the lower 95% confidence interval (CI) of the hazard ratio (HR) of WBRT vs no WBRT was not below 0.9.

RESULTS PP analysis showed that patients treated with WBRT experienced benefit in terms of PFS (not statistically significant): 18.2 vs 11.9 months, HR 0.83 (95% CI 0.65–1.06), but without effect on OS: median 32.4 months with WBRT vs 37.1 months without WBRT, HR 1.03 (95% CI 0.79–1.35). ITT analysis showed similar results as WBRT significantly helped prolong PFS (15.4 vs 9.9 months, HR 0.79, 95% CI 0.64–0.98), whereas no difference in OS was found (32.4 vs 36.1 months, HR 0.98, 95% CI 0.79–1.26). In the as-treated analysis, WBRT
significantly improved PFS from last HDMTX in patients with complete response (HR 0.64, 95% CI 0.44–0.94), but not OS (HR 0.93, 95% CI 0.68–1.53). In patients without complete response, there was significant difference in PFS from last HDMTX among patients treated with WBRT (15.9 months), HD-Ara-C (3.2 months), and no further therapy (8.9 months); HR 0.47 (95% CI 0.35–0.62). There was no significant OS difference among the 3 groups, however; HR 0.76 (95% CI 0.56–1.02).

The study failed to prove NI of HDMTX without WBRT to HDMTX with WBRT, as shown in the figure, given that all lower limits of the CIs were smaller than 0.9.

**INTERPRETATION AND DISCUSSION**

PCNSL is an uncommon aggressive variant of NHL. HDMTX is the most important drug for the treatment of PCNSL. A few studies have suggested polychemotherapy, combining HDMTX with cytarabine, ifosfamide, or vincristine. Moreover, the role of rituximab in PCNSL is currently being investigated in randomized trials. Consolidation of chemotherapy with autologous stem cell transplantation or with mechanisms to disrupt the blood–brain barrier has been utilized in clinical practice as well. The role of adding WBRT has been questioned as WBRT is linked to delayed neurotoxicity in up to 75% in patients over age 65. Thus, this recently published article in *Neurology* evaluated whether a regimen of HDMTX without WBRT was noninferior to a regimen with WBRT.

We herein elaborate on issues related to NI trials. NI trials prespecify NI margins (M). Under the null hypothesis for NI trials, the difference between the standard and experimental treatment is larger than or equal to M, whereas the difference is less than M under the alternative hypothesis: \( H_0: S - T \geq M \) (treatment T is inferior to the standard S by M or more); \( H_a: S - T < M \) (T is inferior to the standard by less than M). The margin can be no larger than the presumed entire effect of the standard treatment; otherwise NI would not represent evidence of any efficacy. The conventional method of choosing a margin compares the upper or lower limit of the 95% CI of the calculated effect to the margin (HR 0.9 in this study). However, given the abovementioned concern of the experimental treatment having no effect, albeit being noninferior to the standard treatment, new approaches for determining the margin have been suggested. The Food and Drug Administration proposed other approaches for NI trials instead of the conventional methods, namely the effect retention or putative placebo approach, and the 95%–95% approach.

This study had only 60% power to prove NI, i.e., 60% probability to conclude NI under the alternative hypothesis, and failed to prove NI.

In superiority trials, ITT analysis represents a conservative approach as protocol violations including crossover and loss to follow-up make results shift toward a no difference conclusion (the null hypothesis in superiority trials and the alternative hypothesis in NI trials). Thus, the role of ITT analysis in NI trials has also been debated. It is favorable that both PP and ITT analyses are reported in NI trials. In this article, the results of PP analysis were similar to the results of ITT and as-treated analyses. In cases of discrepancies, it is advised to follow the more conservative results.

The study was the largest and only phase III trial to date in PCNSL, and was difficult to execute. As the authors acknowledge, the study had a number of limitations, and there were considerable protocol violations and loss to follow-up. First, there was high mortality during HDMTX chemotherapy, and thus the protocol was amended to add ifosfamide to the initial regimen. This was not controlled for in the analysis, however, as the authors did not include data comparing percentage of CR, or measurements of PFS/OS, before and after adding ifosfamide. Crossover is another important violation of the study protocol. Only 65% of patients who achieved CR in the HDMTX + RT group received intended therapy and 7% of patients without CR received chemotherapy. On the other hand, nearly 100% of patients who achieved CR in the HDMTX alone group received intended therapy and 28% of patients with no CR received WBRT. Hence, crossover occurred much more frequently in patients who did not achieve CR, which can significantly impact the conclusions.
from the study. Finally, 63% of patients in the HDMTX alone group who did not achieve CR received HD-Ara-C, which is yet another confounder that was not controlled for; salvage therapy data are important in studies demonstrating PFS benefit with no OS benefit.

Overall, the study showed that WBRT could delay relapse in patients with PCNSL after treatment with HDMTX, at the price of delayed neurotoxicity. The final updated version of the clinical trial did not include data about neurocognitive endpoints, however. The initial report, published in 2010, included data for clinically defined neurotoxicity in 79 patients, and for radiologic-defined neurotoxicity in 84 patients after a median follow-up of almost 50 months. Signs of neurotoxicity were observed more frequently in patients who underwent WBRT, with p values of 0.054 and 0.04, respectively.² Risks and benefits for each patient, given certain age and comorbidities, as well as whether or not the patient achieved complete response after initial HDMTX, should be weighed before making a decision about following HDMTX with WBRT as consolidation or salvage therapy.

AUTHOR CONTRIBUTIONS
Iyad Alnahhas, neurology PGY2 resident, appraised the original article and wrote the manuscript under the supervision of Dr. Mark Malkin, who edited the contents and discussion of the final submitted version.

STUDY FUNDING
No targeted funding reported.

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

REFERENCES
Media and Book Review

The *Neurology* offices frequently receive newly published books, and residents and fellows are invited to review these. Reviewers will be allowed to keep the books. Reviews should be 250-500 words, and include the strengths and weaknesses of books for a trainee audience. Interested individuals should contact the journal at rwitherow@neurology.org for available books to review. We also welcome reviews of on-line, electronic, and other educational materials, and interested individuals should contact the journal to discuss their ideas.
REACHING DOWN THE RABBIT HOLE: EXTRAORDINARY JOURNEYS INTO THE HUMAN BRAIN


Allan Ropper’s Reaching Down the Rabbit Hole: Extraordinary Journeys into the Human Brain, cowritten with Brian Burrell, is a first-person narrative about hospital neurology. Popular science is a staple of nonfiction publishing and the mysteriousness of neurologic disease is the hook of the subtitle “Extraordinary journeys into the human brain.” For nonprofessional readers, the idea of Allan H. Ropper as a real-life version of Dr. Gregory House, the unconventional Sherlock Holmes–like medical character on TV, is a seductive one.

While Lewis Carroll’s Alice’s Adventures in Wonderland is the source of the title, the theme of implausible reality in neurologic practice comes from the White Queen of Through the Looking-Glass. Neurology is queen of the medical specialties, says Ropper. Like Wells, a queen among Gothic cathedrals, she is neither the biggest nor necessarily the best but few exceed her for finesse and elegance.

Popular culture neurologists are an unrepresentatively extroverted sample. Oliver Sacks is the best known, although Ropper’s book has more affinity with those of the Chicago neurologist–writer Harold Klawans by its references to baseball lore and supporting cast of hospital doctors. Among them is Elliott, the neurologist with whom Ropper shares his term of ward duty, who is his temperamental opposite. With his dispassionate thoughtfulness and distancing strategies, Elliott has the aloofness that is common among neurologists. Has it developed out of our professional work or did we have it before neurology?

Reaching Down the Rabbit Hole does not particularly try to be funny, yet its commentary on how events happen to arrange themselves has a comic sensibility. Ropper’s mirthless exchange of one-liner jokes with a hospital visitor who turns out to be a former comedy writer establishes a fellowship between the men and helps us understand the origins of this show business take on clinical neurology.

Ropper solves case after case, but criticism that Reaching Down the Rabbit Hole is short on professional humility is not entirely fair. His initial diagnosis of a patient with acute quadriplegia is wrong, and events then unfold too rapidly to avert catastrophe. Ropper is reminded of fallibilities that will trip up even an expert. He is in thrall to the buzz of the Sherlock Holmes moment of grasping the diagnosis from the barest of facts, deaf to Watson’s cautionary voice in his head, and he fails to mitigate the fatal flaw of hubris.

Elliott quotes F. Scott Fitzgerald’s The Great Gatsby (“So we beat on, boats against the current.”) to introduce a meditation about progress and generational change. Jay Gatsby and the White Queen share the conviction that you can project your memories into your future. As Nick Carraway tries to tell Gatsby, “You can’t repeat the past.” Now near the end of his own career, Ropper reflects on his mentors and the passing of time. He foreshadows a neurology that has followed some of the kings of the medical specialties into a new world of technology and process, stripped of her traditional craft skills. The main message of this book of neurologic anecdotes is about stories themselves, and an intellectual curiosity in their content and significance.

Reviewed by Peter A. Kempster

Disclosure: The author reports no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

© 2015 American Academy of Neurology
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: 
A 21-year-old man with visual loss following marijuana use

SECTION 1
A 21-year-old man with no reported medical history presented to the emergency department complaining of bilateral blurry vision. His symptoms began abruptly 2 days prior to presentation, preceded by a thunderclap headache the week prior. Initial evaluation at an outside emergency department found a urine drug screen positive for cannabis, and his symptoms were misattributed to marijuana intoxication. The patient was a chronic, daily marijuana user. There was no family history of migraine, early-onset cerebrovascular or cardiovascular disease, or hypercoagulable state.

The neurologic examination was notable for uncorrected near visual acuity of 20/30 bilaterally. A right homonymous hemianopia was found on confrontational visual field testing. Pupillary reactivity and ocular motility was normal. No papilledema was evident. Facial and palatoglossal movements were normal. The patient was unable to read simple or complex sentences. Writing, fluency, repetition, comprehension, and object naming were intact. The remainder of the neurologic examination had normal results. There were no dermatologic or ocular abnormalities.

Questions for consideration:
1. What is the most likely neuroanatomic localization based on the examination findings?
2. What differential diagnoses should be considered at this point?
SECTION 2
Right homonymous hemianopia localizes to the ret- 
rochiasmal afferent visual pathway (optic tract, optic 
radiation, or primary visual cortex) in the left hemi-
sphere. The inability to read with preserved writing 
is termed “alexia without agraphia,” which is a dis-
connection syndrome caused by involvement of the 
splenium of the corpus callosum. A lesion involving 
the left occipital cortex and adjacent splenium func-
tionally disconnects the intact right hemispheric 
visual cortex from the left hemispheric language areas 
necessary for reading; this deficit is seen in left poste-
rrior cerebral artery (PCA) distribution infarcts. Ad-
ditional clinical findings associated with left PCA 
infarction include hemichromatopsia (impaired 
color vision), palinopsia, micropsia, macropsia (visu-
opsychic phenomena characterized by persistent 
image in the blind hemifield, and appearance of ob-
jects smaller or larger than expected, respectively), 
visual agnosia, Gerstmann syndrome (acalculia, 
agaphia, finger agnosia and right-left confusion), 
and aphasia (anomic or transcortical sensory).1 Occa-
sionally a single trunk off the PCA (artery of Perche-
ron) supplies the bilateral thalamus and midbrain; in 
such cases, infarction is hallmarked by lethargy, mem-
ory disturbance, thalamic aphasia, sensorimotor 
impairment, and ophthalmoplegia.

Abrupt symptom onset should prompt consider-
ation of a vascular etiology such as ischemic or hemor-
 rhagic stroke. The heralding thunderclap headache 
raises the possibility of subarachnoid hemorrhage, cer-
vicocephalic dissection, cerebral venous thrombosis, or 
reversible cerebral vasoconstrictive syndrome. Primary 
or secondary complications related to marijuana or 
other illicit substances are considerations. Infectious, 
neoplastic, and demyelinating processes warrant con-
sideration but were believed to be less likely.

Brain MRI with and without contrast showed 
aacute bihemispheric infarction in multiple arterial ter-
ritories (figure). The left PCA distribution acute 
infarction involved the visual cortex and splenium 
of the corpus callosum resulting in the clinical syn-
drome of alexia without agraphia. Gradient-echo 
sequences were unremarkable. Four-vessel cerebral 
angiogram was normal. Laboratory testing was 
remarkable for a serum creatinine of 1.2 and EKG 
demonstrated a right bundle branch block. Evaluation 
with transthoracic and transesophageal echocardio-
gram and cardiac MRI were normal. Investigation 
for inherited or acquired prothrombotic states re-
ealed heterozygosity for MTHFR mutation; homo-
cysteine level was normal.

Questions for consideration:
1. What are the most common causes of stroke in the 
young?
2. What is the relationship between marijuana use 
and stroke?
Approximately 5% of strokes occur in young adults age 15–45 years. In young adults with arterial ischemic stroke (AIS), cardioembolism accounts for 20%–30%, cervicocephalic dissection 10%–25%, premature large-artery atherosclerosis 8%, small vessel disease 14%, vasculitis 7%, reversible cerebral vasoconstriction syndrome 1%, and Moyamoya 1%. Prothrombotic states, inherited causes, substance abuse, transient cerebral arteriopathy, and postinfectious vasculopathy (varicella-zoster virus) are also important considerations. Cervicocephalic dissection may be associated with fibromuscular dysplasia, Ehlers-Danlos syndrome, Marfan syndrome, coarctation of the aorta, and Moyamoya. A bimodal age distribution is seen in Moyamoya with pediatric populations (first decade of life) and in adults age 30–40 years. The incidence of pediatric Moyamoya in the United States is 0.086 per 100,000, although the incidence increases in Asians and African Americans. This entity accounts for roughly 6% of childhood AIS in Western countries. Genetic susceptibility should be considered in young patients with stroke; a family history of stroke should prompt consideration of monogenic disorders that include stroke as a phenotype. Sickle cell disease is a significant hematologic contributor to arterial stroke due to prothrombotic state and progressive vasculopathy. The frequency of factor V Leiden mutation and antiphospholipid syndrome is 8% and 6%, respectively. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy is seen in 1%, similar to mitochondrial disorders (1%). The incidence of Fabry disease (FD) in young adults with unexplained stroke may be up to 1.2%.

Active malignancy leading to prothrombotic state is thought to contribute 1% of stroke. Drug-induced AIS has a similar frequency of 1%. Migraine is another risk factor, thought to be the cause in 1%–5%. Despite thorough testing, cryptogenic stroke accounts for approximately one-third of AIS in both young adults and children.

The association between marijuana use and stroke is unclear; fewer than 60 cases have been reported citing a temporal relationship. A causal relationship has not been established, largely due to lack of extensive neurovascular imaging and confounding factors including lifestyle and genetic predisposition. Postulated downstream effects of cannabis include impaired cerebral autoregulation, labile blood pressure, cardiac arrhythmias, vasculopathy, vasospasm, reversible cerebral vasoconstriction syndrome, and multifocal intracranial stenosis. The latter 2 are strong considerations in the mechanical pathogenesis of stroke associated with marijuana use.

Additional family history was elicited; the patient’s sister developed progressive visual deterioration and painful acroparesthesias during adolescence. A maternal half-uncle developed early-onset renal failure requiring hemodialysis at age 32 years. The patient was able to recall a personal history of painful acroparesthesias beginning in adolescence.

Question for consideration:

1. What additional testing should be considered in light of the family history?
Enzyme replacement therapy (ERT) is costly but improves life expectancy to the fifth or sixth decade. ERT has yet to be proven to reduce future stroke risk. ERT should be considered for patients with FD in addition to antiplatelet therapy, blood pressure reduction, glycemic control, and lipid lowering for those with stroke. Clinical trials using pharmacologic chaperone therapy to facilitate proper tertiary structure of α-galactosidase A show increased GLA activity and reduced Gb-3 accumulation in multiple organ systems. Chaperone therapy appears to be effective in mutations causing protein misfolding but is not effective for all mutations resulting in FD.

Clinicians should retain a high index of suspicion for FD when evaluating stroke in the young, given the multisystem involvement and the need for comprehensive multispecialty care for the best prognosis.

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.

All the respondents for this Mystery Case identified the patient’s clinical syndrome as pure alexia—also known as alexia without agraphia—and localized this syndrome to the dominant occipital lobe and splenium of the corpus callosum. A total of 75% of respondents recognized that the patient’s clinical findings and family history are suggestive of FD; each of these respondents correctly identified α-galactosidase activity as the appropriate diagnostic test for this disorder.

The most complete answer came from Jeremy Cutsforth-Gregory from Mayo Clinic, who noted that the diagnostic test of choice for female patients is molecular genetic testing of the GLA gene. In heterozygous females, α-galactosidase activity is an unreliable indicator and may be within the normal range.

This case highlights a rare but treatable disorder with both neurologic and systemic manifestations, and underscores the importance of screening for systemic involvement to reach an accurate diagnosis.

Andrew Schepmyer, MD
University of British Columbia

Thank you to the Editor-in-Chief and Executive Editor

The Neurology Resident & Fellow Editors would like to thank Editor-in-Chief Dr. Robert Gross and Executive Editor Patty Baskin for their continued support.
Opinion & Special Articles

These articles provide timely opinions about important areas in neurology education and training. Relevant topics include medical student teaching, training requirements, work/life balance, board certification, and directions in education. Seeking the assistance of senior faculty members is often useful. Those interested in writing these manuscripts should contact the Resident & Fellow Section editor before submission to inquire about the interest in specific topics.
Neuroinfectious diseases is an emerging subspecialty of neurology.¹ We are seeing an increasingly immunocompromised patient population due to advances in transplant medicine and novel treatments for autoimmune disorders and cancer. This growing group of high-risk patients, in combination with a rise in international travel, has expanded the quantity and spectrum of infections of the nervous system. Substantial progress in molecular diagnostic testing has resulted in greater awareness of pathogens able to cause neurologic infections. While neurologic opportunistic infections in HIV-infected individuals are often deadly complications, a new set of challenges has arisen in HIV-infected individuals with well-controlled disease.

The socioeconomic burden of neuroinfectious diseases is enormous. Patients often require lengthy hospitalizations, extensive diagnostic evaluations, long-term antimicrobial therapy, and prolonged rehabilitation.² As such, the care of neuroinfectious diseases requires collaboration among various areas of expertise, including neurology, infectious diseases, HIV medicine, and microbiology. Clinicians with experience and training in neuroinfectious diseases possess a unique perspective, distinct set of skills, and specialized fund of knowledge to provide high-quality care for these patients. This unique skill set and fund of knowledge represent a knowledge gap among practicing neurologists that should be an important focus of current residency training.

As a joint effort between the Department of Neurology and Division of Infectious Diseases at the University of California, San Francisco (UCSF), we recently created an interdisciplinary neuroinfectious diseases clinic serving the local and surrounding communities with a focus on the care of individuals with infections of the nervous system and neurologic complications of HIV. We describe our efforts to develop a one-of-a-kind clinical and training experience in order to provide expert care and to fill this knowledge gap among practicing neurologists.

CLINIC STRUCTURE AND PATIENT POPULATION The neuroinfectious diseases clinic was established within the general infectious diseases outpatient clinic in July 2012 by a neurologist with infectious diseases subspecialty training (F.C.C.). This neuroinfectious diseases faculty member is directly embedded in the infectious diseases clinic. Between July 2012 and March 2014, we saw 44 new consultations in our monthly clinic. Referrals were accepted if they had an established infection of the nervous system, if there was a high degree of suspicion for an infection, or if they were HIV-infected with a neurologic chief complaint. The mean age of the patients was 47.6 years (SD 15.2 years) and ranged from 20 to 79 years. Fourteen (32%) of the 44 new patients were women and 18 (41%) were of nonwhite race/ethnicity. Twenty-one (48%) patients were HIV-infected. Of the 23 non-HIV-infected patients, 7 were immunocompromised (3 due to malignancy, 1 from chronic corticosteroid use, 1 from treatment for multiple sclerosis, 1 due to a renal transplant, and 1 from diabetes mellitus). Six patients were immigrants and 3 were returning travelers.

REFERRAL PATTERNS Referrals originated from the infectious diseases consult team for patients seen in the hospital who required outpatient follow-up, the neurology or neurosurgery inpatient service, HIV primary care clinics, and general neurology or other neurology subspecialty clinics (e.g., neuro-oncology, multiple sclerosis clinic). Ten patients were referred by outside physicians. Most patients were seen within 1 month of referral, and the majority of patients (more than 80%) were followed over multiple visits.

PATIENT CASE MIX A wide range of diagnoses was seen in the clinic (table). Among immunocompetent patients, diagnoses included pyogenic brain infections and fungal and viral meningitis. Neurocysticercosis was the most common diagnosis in immigrants and returning travelers. For non-HIV-infected immunocompromised

From the Department of Neurology (F.C.C., S.A.J.) and Department of Medicine, Division of Infectious Diseases (B.S.S.), University of California, San Francisco.

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.
patients, diagnoses included *Nocardia* brain abscesses and Epstein-Barr virus encephalitis. Of the 21 HIV-infected individuals, 10 (48%) had incompletely controlled HIV and were primarily seen for HIV-associated neurologic infections, including progressive multifocal leukoencephalopathy and CNS toxoplasmosis. Of those whose HIV viral load was suppressed, frequent neurologic complaints included headache, seizure, and cognitive impairment.

For half of the new patients seen in the clinic, a definitive diagnosis was already established at the time of referral, while the remainder presented without a known diagnosis. Nearly half (48%) of patients were actively treated with antimicrobial therapy as part of an outpatient management plan, while 30% received only symptomatic management (e.g., pain control, seizure management). A small subset of patients was referred for a specific diagnostic or prognostic question (e.g., lumbar puncture to rule out neurosyphilis or neurologic prognosis following viral encephalitis) that did not require long-term follow-up.

**TRAINEE INVOLVEMENT** Neurology trainees have been incorporated into the clinic and independently see new consultations (2–3 per clinic) and discuss cases with the attending, in addition to observing follow-up visits. Fellows in the UCSF HIV Neurology Research Training Program also have the option to rotate through the clinic as part of their clinical training. Visiting international residents and medical students participate largely in an observatory role.

The resident experience in the clinic is one component of a neuroinfectious diseases elective designed to provide UCSF residents with broad exposure to the diagnosis and management of infections of the nervous system and neurologic complications of HIV. In addition to rotating in the neuroinfectious diseases clinic, residents are able to spend time on the inpatient consult infectious disease teams, in an outpatient tuberculosis clinic, in an HIV-associated cognitive impairment clinic, and in an HIV urgent care clinic. Similar clinical experiences are available to fellows in the HIV Neurology Research Training Program who are interested in more rigorous clinical

<table>
<thead>
<tr>
<th>Table</th>
<th>Diagnoses seen in a neuroinfectious diseases clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunocompetent patients</strong></td>
<td></td>
</tr>
<tr>
<td>Diagnoses</td>
<td></td>
</tr>
<tr>
<td><strong>Bacterial</strong></td>
<td></td>
</tr>
<tr>
<td>Pyogenic brain abscess with associated seizures</td>
<td></td>
</tr>
<tr>
<td>Pyogenic bacterial meningitis with associated strokes</td>
<td></td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td></td>
</tr>
<tr>
<td><strong>Fungal</strong></td>
<td></td>
</tr>
<tr>
<td>Coccidioidal meningitis (2)</td>
<td></td>
</tr>
<tr>
<td>Sporothrix meningitis</td>
<td></td>
</tr>
<tr>
<td>Histoplasma meningitis</td>
<td></td>
</tr>
<tr>
<td>Subacute meningitis, presumed fungal</td>
<td></td>
</tr>
<tr>
<td><strong>Viral</strong></td>
<td></td>
</tr>
<tr>
<td>HSV-2 meningitis</td>
<td></td>
</tr>
<tr>
<td>VZV meningitis</td>
<td></td>
</tr>
<tr>
<td>West Nile virus</td>
<td></td>
</tr>
<tr>
<td><strong>Parasitic</strong></td>
<td></td>
</tr>
<tr>
<td>Neurocysticercosis (4)</td>
<td></td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic meningencephalitis, unknown etiology</td>
<td></td>
</tr>
<tr>
<td>Neuropathy, rule out infectious cause</td>
<td></td>
</tr>
<tr>
<td><strong>Immunocompromised (non-HIV) patients</strong></td>
<td></td>
</tr>
<tr>
<td>Diagnoses</td>
<td></td>
</tr>
<tr>
<td><strong>Bacterial</strong></td>
<td></td>
</tr>
<tr>
<td><em>Nocardia</em> brain abscess (2)</td>
<td></td>
</tr>
<tr>
<td>Pyogenic bacterial meningitis</td>
<td></td>
</tr>
<tr>
<td><strong>Viral</strong></td>
<td></td>
</tr>
<tr>
<td>EBV encephalitis</td>
<td></td>
</tr>
<tr>
<td>PML</td>
<td></td>
</tr>
<tr>
<td><strong>Fungal</strong></td>
<td></td>
</tr>
<tr>
<td>Sporothrix meningitis</td>
<td></td>
</tr>
<tr>
<td><strong>Unknown</strong></td>
<td></td>
</tr>
<tr>
<td>Chronic meningencephalitis, unknown etiology</td>
<td></td>
</tr>
<tr>
<td><strong>HIV-infected patients</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Infectious</strong></td>
<td></td>
</tr>
<tr>
<td>PML/PML IRIS (2)</td>
<td></td>
</tr>
<tr>
<td>Cryptococcal meningitis/IRIS (2)</td>
<td></td>
</tr>
<tr>
<td>CNS toxoplasmosis with associated seizure</td>
<td></td>
</tr>
<tr>
<td>HIV CNS escape</td>
<td></td>
</tr>
<tr>
<td>Neurosyphilis (2)</td>
<td></td>
</tr>
<tr>
<td><strong>Noninfectious</strong></td>
<td></td>
</tr>
<tr>
<td>Myelopathy</td>
<td></td>
</tr>
<tr>
<td>Myopathy + cognitive impairment</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment (3)</td>
<td></td>
</tr>
<tr>
<td>Seizure (2)</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations: EBV = Epstein-Barr virus; HSV = herpes simplex virus; IRIS = immune reconstitution inflammatory syndrome; PML = progressive multifocal leukoencephalopathy; VZV = varicella-zoster virus.*
training. HIV Neurology fellows supervise residents at a county hospital, where neuroinfectious diseases are a common diagnosis, and also lecture on neuroinfectious diseases topics in the residency core curriculum. These fellows are involved in longitudinal research projects in which interested residents can also participate as either an elective experience or as part of a broader flexible residency project.

As part of the neuroinfectious diseases elective, residents are expected to independently evaluate patients and synthesize and interpret clinical data, while working closely with an attending physician from various disciplines, including infectious diseases, HIV medicine, and neurology. Residents also gain experience in communicating and maintaining a professional and productive working relationship with health care providers in non-neurologic fields and in interdisciplinary settings. In addition to clinical teaching and feedback, dedicated didactics include small group lectures, one-on-one case-based teaching with an attending physician in neuroinfectious diseases, microbiology plate rounds, and grand rounds in infectious diseases and HIV. Each rotating resident is exposed to a set curriculum of topics that are complemented by direct patient contact.

**DISCUSSION** The neuroinfectious diseases clinic at UCSF, a joint effort between neurology and infectious diseases, delivers subspecialty outpatient care to patients with infections of the nervous system and HIV-infected individuals with neurologic disease. Interdisciplinary neuroinfectious diseases clinics, even in major academic medical centers, are rare. Services provided by neuroinfectious diseases clinicians through this type of clinic include management of antimicrobial therapy, symptomatic and supportive treatment of neurologic sequelae of infections, and prognostication after debilitating infections of the CNS. Strengths of the clinic include harnessing and developing expertise in a unique and emerging field of neurology, offering prompt access to subspecialty care, and affording an unmatched training opportunity for medical students, residents, and fellows with the goal of filling the knowledge gap in neuroinfectious diseases among neurologists.

We care for a broad array of diagnoses in the clinic, ranging from CNS infections in immunocompromised hosts to more common neurologic complaints in HIV-infected individuals. While new diagnoses are made in clinic, a substantial proportion of patients present to the clinic with a known diagnosis. In our experience, a primary service of the clinic is to provide longitudinal outpatient management of established, often immensely complicated neurologic infections and associated sequelae. Indeed, neuroinfectious diseases clinicians are one of many examples of the movement of neurologists toward a paradigm where they are actively engaged in the longitudinal treatment and prevention of neurologic disease.

The wide range of pathology and diverse patient population seen in the clinic result in a unique learning opportunity for neurology trainees in neuroinfectious diseases. Overall, the educational goals for trainees rotating through the neuroinfectious diseases clinic and elective, adapted from the American Academy of Neurology neuroinfectious diseases subspecialty training core curriculum, are to (1) formulate a differential diagnosis, including potential causative pathogens, for common neurologic infectious syndromes (i.e., meningitis, encephalitis, brain abscess) in the immunocompetent and immunocompromised host; (2) devise a systematic approach to common neurologic sequelae (e.g., seizures, headache, cognitive impairment) of infections, including HIV; (3) develop a working knowledge of the utility and validity of various laboratory tests in the serum and CSF when a CNS infection is suspected; (4) recognize the role of specific imaging techniques, including restricted diffusion and postcontrast sequences, in distinguishing between infections and other processes; and (5) understand the principles of antimicrobial therapy, including antibiotic selection and frequently encountered drug–drug interactions and enhanced toxicities with combinations of antimicrobials and medications regularly used to treat neurologic disease (e.g., antiepileptic drugs, neuropathic pain agents). Simple metrics are used to gauge progress toward meeting these educational goals through one-on-one discussions of patients and didactic cases as well as during lectures. Administration of a neuroinfectious diseases pretest and post-test may also help in the future to quantify the knowledge obtained from rotating in the clinic.

Establishing an interdisciplinary neuroinfectious diseases clinic at UCSF has successfully allowed neurology and infectious diseases groups to partner together to provide a clinical service to patients and to fill a knowledge gap in neuroinfectious diseases and HIV neurology among practicing neurologists. This clinic may serve as an example of interdisciplinary collaboration in neurology that benefits patients and trainees alike in complex systems of care that increasingly require this type of partnership to deliver high-quality care.

**AUTHOR CONTRIBUTIONS**

Dr. Chow participated in the study concept and design, performed the data analysis and interpretation, and drafted the manuscript. Dr. Schwartz participated in the study concept and design and provided critical revisions to the article. Dr. Josephson participated in the study concept and design, supervised the study, and provided critical revisions to the article.
STUDY FUNDING
Supported by NIH 5T32MH090847 (F.C.C.).

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

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: Pisa syndrome
An unusual feature of adult-onset fulminant SSPE

PEARLS

• Subacute sclerosing panencephalitis (SSPE) is a delayed, almost invariably fatal, widespread inflammatory response to a defective, persistent, intracellular measles virus infection.

• SSPE commonly presents with a combination of cognitive impairment, cortical blindness, slow myoclonus, and seizures.

OY-STERS

• Parkinsonism is an uncommon initial manifestation of SSPE seen in approximately 5% of patients.

• Pisa syndrome (pleurothotonus) is a rare extrapyramidal manifestation of SSPE and may be confused with young-onset Parkinson disease and related syndromes.

• Myoclonus in such patients may be misinterpreted to be part of a genetic parkinsonian syndrome.

CASE REPORT

A 25-year-old man was referred to our department, a tertiary care neurology facility, with complaints of slowness of movements and a body tilt to the right for 3 months. These complaints were accompanied by multiple falls and behavioral changes, including apathy, lack of self-care, and decreased verbal output. He had a history of high-grade fever lasting for 5 days prior to onset of these symptoms. The patient had a history of measles at age 3 years; he had not been vaccinated owing to sociocultural beliefs. The family history was not suggestive of juvenile parkinsonism, Huntington disease, genetic dystonias, or spinocerebellar ataxias.

On examination, the patient was conscious but apathetic, with masked facies and a blink rate of 9–10 per minute. The vital parameters were normal and there was no postural drop in blood pressure. There was decreased verbal output with intact comprehension for simple commands. He had a history of high-grade fever lasting for 5 days prior to onset of these symptoms. The patient had a history of measles at age 3 years; he had not been vaccinated owing to sociocultural beliefs. The family history was not suggestive of juvenile parkinsonism, Huntington disease, genetic dystonias, or spinocerebellar ataxias.

On examination, the patient was conscious but apathetic, with masked facies and a blink rate of 9–10 per minute. The vital parameters were normal and there was no postural drop in blood pressure. There was decreased verbal output with intact comprehension for simple commands. Mini Mental State Examination score was 20/30. The range of ocular movements was full with slowing of saccades. Rigidity without cogwheeling was present in all 4 limbs while the power was normal. Involuntary shock-like movements involving the trunk and limbs (left > right) were noted. The deep tendon jerks and superficial reflexes were normal. There were no frontal release signs. Bradykinesia was present while the pull test was positive. Gait analysis revealed a relatively wide-spaced stance with small, hesitant steps. The gait was interrupted by myoclonic jerks (video on the Neurology® Web site at Neurology.org).

Hemogram, blood sugar, liver function tests, renal function tests, and thyroid function tests were normal. Enzyme-linked immunosorbent assay for HIV and tests for hepatitis B and hepatitis C viruses were also negative. EEG revealed a background of an average 20 \( \mu \)V amplitude \( \alpha \) activity, interrupted by generalized periodic bursts of stereotypic high-amplitude slow wave R complexes occurring every 2–3 seconds (figure e-1).

CSF analysis revealed 10 cells, all lymphocytes, protein 28 mg/dL, and sugar 85 mg/dL, with corresponding blood sugar of 103 mg/dL. CSF immunoglobulin G antimeasles antibody titers were 23.05 Novatech units (NTU) (normal < 9 NTU, indeterminate 9–11 NTU, increased > 11 NTU; Novatech Immune Diagnostica GmbH, Germany). CSF was negative for other viral markers. MRI of the brain showed subcortical white matter hyperintensities involving the frontal, parietal, and occipital regions on T2-weighted and fluid-attenuated inversion recovery sequences; no contrast enhancement was observed.

The patient was initiated on clonazepam and trihexyphenidyl, and the dosage was titrated to 3 mg of clonazepam in 3 divided doses and 12 mg of trihexyphenidyl in 3 divided doses. He was also administered interferon-\( \alpha \) 6 million units intrathecally, once a week.

The patient had a rapidly progressive downhill course. He became bedbound in 10 days and died on the 26th day of admission. Genetic test reports, available posthumously, revealed heterozygous \( 7LR3 \) (Toll-like receptor 3) gene polymorphisms involving rs3775290, rs3775291, and rs3775296.

From the Department of Neurology, King George’s Medical University, Lucknow, India.

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.
DISCUSSION A mutated measles virus that can remain dormant intracellularly for up to a decade causes SSPE. The reactivation occurs due to an unknown trigger and leads to widespread inflammatory neuronal damage.\textsuperscript{1} It is clinically characterized by rapidly progressive cognitive impairment, scholastic backwardness, behavioral changes, seizures, myoclonic jerks, extrapyramidal involvement, language disturbances, optic atrophy, macular degeneration, and cortical blindness, in variable combinations.\textsuperscript{2} SSPE has been observed to be more common in males, in those with history of measles at less than 2 years of age, and in situations lacking adequate vaccination against measles. Adult-onset SSPE is not significantly different from childhood-onset SSPE except that the latency of measles virus activation is more prolonged in adult SSPE.\textsuperscript{2,3} Our patient had not been vaccinated, and had a history of childhood measles, as well. In its typical form, most patients with SSPE survive for about 18 months (range 1–3 years); our patient had the fulminant form of SSPE where death occurs by 6 months of diagnosis.

Pisa syndrome is an uncommon form of truncal dystonia characterized by lateral bending of the trunk or pleurothotonus. It was first described by Swedish neurologist Karl Axel Ekbom and colleagues\textsuperscript{4} as an untoward reaction to haloperidol in an elderly woman. The etiology, Pisa syndrome, owes its inspiration to the famous leaning tower of Pisa in Italy for its unintended 5.5° tilt. It is clinically defined as a lateral flexion of more than 10° in the standing position due to axial dystonia.\textsuperscript{5} After the initial documentation as an adverse drug reaction, this syndrome has been observed in several disorders, such as Parkinson disease, multiple system atrophy, and as a reaction to neuroleptics.\textsuperscript{5,7}

The exact pathogenesis of Pisa syndrome remains elusive, and many theories have been postulated. Women and elderly with organic brain disease appear to be at increased risk.\textsuperscript{7} It can occur as an acute dystonic reaction and more commonly as an atypical form of tardive dystonia. The response to anticholinergics and reduction or withdrawal of neuroleptics suggest the possible role of cholinergic excess or imbalance between cholinergic and dopaminergic neurotransmission in the development of this rare syndrome.\textsuperscript{5,7} The abnormality in recruitment of truncal muscles or abnormal proprioceptive motor control have also been postulated as major reasons behind Pisa syndrome in Parkinson disease.\textsuperscript{5} The marked hyperactivity in the paraspinal muscles on the less affected side is considered another plausible cause for Pisa syndrome in Parkinson disease. Tassorelli et al.\textsuperscript{8} observed that Pisa syndrome occurs in patients with advanced disease and in those with marked asymmetry; the bending is usually noted contralateral to the onset of the disease. In their series, almost 40% of patients responded to anticholinergic therapy. It may be noted that only acute dystonic reactions might respond to anticholinergics and not the more commonly observed tardive dystonias, which typically worsen with anticholinergics; clonazepam may serve as an alternative in the latter category.
Dystonia and parkinsonism are uncommon manifestations of SSPE. In a series of adult-onset SSPE, myoclonus was the commonest presentation and extrapyramidal symptoms were observed in only 2 of 39 patients (5.1%). Recently, status dystonicus and rhabdomyolysis were reported in a patient with SSPE occurring secondary to pneumonia. Misra et al. reported 2 adolescents with SSPE who presented with parkinsonian features prior to myoclonic jerks. To our knowledge, Pisa syndrome has not been described in the literature in association with SSPE; it should be considered in patients presenting with a new focal dystonia and rapid cognitive decline.

In a study of 40 patients with SSPE, it has been concluded that the TLR3 gene may confer host genetic susceptibility to SSPE in Japanese individuals. Our patient was detected having heterozygous TLR3 gene polymorphism affecting rs3775290, rs3775291, and rs3775296, simultaneously, which has not been observed earlier. Whether this simultaneous occurrence, vis-a-vis single TLR3 polymorphism, portends a fulminant course needs to be seen in more patients with SSPE.

Pisa syndrome is a novel presentation of SSPE that may be confused with genetically determined parkinsonian syndromes on the background of adult onset of symptoms and subtle myoclonus. This case is also atypical for its fulminant and fatal course. SSPE should be added to the list of causes of Pisa syndrome.

STUDY FUNDING
No targeted funding reported.

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: Determinants of burnout of neurology trainees in Attica, Greece

ABSTRACT

Objective: The purpose of our cross-sectional study was to estimate the rate of burnout and identify its determinants among neurology residents in Attica, Greece.

Methods: In total, 131 placements for neurology training over 18 hospitals were available. All residents were approached and were asked to participate in the study by anonymously completing a questionnaire. Job demands and resources (JD-R) were examined via a 31-item questionnaire assessing 8 factors based on the JD-R model. Burnout was measured with the Maslach Burnout Inventory (MBI). The emotional exhaustion criterion was used to distinguish respondents with and without burnout.

Results: A total of 116 residents participated in the study (response rate 88.5%). In total, 18.1% of the participants were experiencing burnout. Multivariate analysis showed that each increased point in the total score of the factor regarding opportunities for professional development was associated with lowering the odds of burnout by 28.7%.

Conclusions: Burnout among neurology residents is associated with decreased professional development. Educators and program directors need to identify those residents at high risk of burnout and design interventions to promote residents’ resilience and mental health. Neurology®

2015;85:e81–e84

GLOSSARY

DP = depersonalization; EE = emotional exhaustion; JD-R = job demands-resources; MBI = Maslach Burnout Inventory; PA = personal accomplishment.

Awareness that trainee doctors are prone to burnout has grown over recent years. The consequences of burnout include less productive working hours, poor quality of life, poor mental health, and increased risk for medical errors.

Several studies have focused on estimating the burnout rates among medical residents, showing that the rates vary among specialties. Neurology not only has a very high rate of burnout but also has the poorest work–life balance.

As proposed by Demerouti et al., in the job demands-resources (JD-R) model, burnout can develop where demands are increased and resources are limited, as such environments can lead to physical exhaustion and reduce the employees’ motivation. Studies that have used the JD-R or similar models among health care professionals have shown that time pressure, lack of autonomy, and lack of opportunities for professional development may lead to burnout as well as increased psychological distress.

The purpose of our cross-sectional study was to estimate the rate of burnout and identify its determinants among neurology trainees in Attica, Greece, using the JD-R model.

METHODS Procedure and participants. Attica is a region covering the metropolitan area of Athens, the capital of Greece. About 3.8 million people live in the region (more than 35% of the total Greek population). Within Attica, 18 hospitals provide neurology training. In total, 131 such placements are available (more than 55% of the total neurology training placements in Greece).

From the Department of Neurology (P.Z., M.L., A.R.), Evangelismos General Hospital; the Department of Neurology (A.K.A.), 417 NIMTS Hospital; the 1st Department of Neurology (A.K.A., S.X.), Agionissiot Hospital, School of Medicine, Kapodistrian University of Athens; the Department of Neurology (E.P.), St. Pantaleimon General State Hospital, Nikia; the Department of Neurology (E.B.), Thriassio General Hospital, Elefsea; and the Department of Psychology (F.A.), Panteion University of Social and Political Sciences, Athens, Greece.

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.
Each item was rated on a 5-point Likert scale ranging from never to always.

All neurology residents in Attica were approached and asked to participate in the study. An anonymous questionnaire was administered to all trainees, who were asked to return it completed in a sealed envelope that was placed in a nontransparent empty box by the participant, in order to ensure the anonymity of the responses. Participation in the study was voluntary.

The study protocol was approved by the local ethics committee.

Measures. Collected data included demographic and other work-related characteristics such as stage of training, true working hours per day, number of on-calls per month, and overall compliance with the European Working Time Directive, which includes a limit set up by the European Working Time Directive.

Job demands and resources were assessed via 31 items, which were rated on a 5-point Likert scale (ranging from never to always). These items were grouped into 8 factors (table 1). The score of each factor was calculated as the sum of its items’ scores. The survey items were subsets of already validated instruments and constituted complete subdomains that were part of the original instruments.

The Maslach Burnout Inventory (MBI), a validated 22-item questionnaire, was used to measure burnout. Each item of the MBI is rated on a 7-point Likert scale (ranging from never to every day). The MBI yields 3 subscale scores (calculated as the sum of its subscale item scores) that assess burnout in relation to its 3 dimensions: emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA). Prins et al. 9 suggested that “the most effective way of diagnosing burnout seems to involve using a system of high scores on both EE and DP, or a high score on EE combined with a low score on PA. Scores ≥75% are considered high and scores ≤25% are considered low.” In keeping with these suggestions, we defined burnout as a high score on EE, accompanied by high DP or low PA (i.e., EE + 1 criterion). Given that there were no established burnout cutoff scores for the Greek version of the MBI, distribution of each subscale score of our study population was divided into quartiles, and high scores meant scoring in the 75th percentile or higher, whereas low scores meant scoring in the 25th percentile or lower. Thus, a high score on both MBI-EE and MBI-DP, or a high score on MBI-EE combined with a low score on MBI-PA, were used to distinguish respondents with and without burnout.

Statistical analysis. A database was developed using the statistical software package SPSS (version 16.0 for Macintosh; Chicago, IL). Descriptive statistics were examined for each variable. Statistical comparisons were performed between the residents with and without burnout concerning demographic characteristics, job demands and resources, and the other measured work-related factors. Categorical variables were compared using the χ² test, normally distributed continuous variables by the Student t test, and non-normally distributed continuous variables by the Mann-Whitney U test.

Where statistically significant differences were found, these variables were entered in the logistic regression model, with burnout being the dependent variable. All accuracy and generalization assumptions for the model were checked. Level of significance was set at the 0.05 level.

RESULTS The study took place between October 2014 and November 2014. A total of 116 residents participated (response rate 88.5%). The study sample had a mean age of 34.5 ± 3.6 years (range 26–45); 64 (55.2%) were women and 69 (59.5%) were single. The mean remaining time to complete neurology training was 18.0 ± 10.8 months, the mean working hours per day, not including on-call duties, was 7.1 ± 1.1 hours, and the mean number of on-calls per month was 4.7 ± 1.7. The number of doctors exceeding the limit set up by the European Working Time Directive was calculated to be 14 (12.1%).
DISCUSSION

The results of this cross-sectional study show that burnout is not uncommon among neurology residents of Attica, Greece. Almost 1 out of 5 residents has burnout syndrome. The novelty of our study is that it was designed to measure burnout specifically among neurology residents.

In their recent review of physician burnout, Sigsbee and Bernat2 highlighted that studies of motivational factors in the workplace suggest several interventions to prevent burnout. These interventions include personal or group counseling, identification and elimination of meaningless required hassle factors, redesign of practice, and creation of a culture that promotes career advancement, mentoring, and recognition of accomplishments.2 In our study, we used the JD-R model, showing, in the univariate analysis, that supervisor support, work–home demands interface, autonomy, and opportunities for professional development were factors significantly associated with burnout among neurology trainees. Thus, our findings may answer some of the fundamental questions set by Busi10 in his editorial, as these findings showed that the stage of training and the working hours do not affect burnout probability, especially when opportunities for professional development remain unhampered.

Our study cannot answer other questions set by Busi,10 such as whether burnout rates, determinants, and characteristics are different between trainee and trained neurologists. Another limitation of our study is that our study population comprised residents in Greek training programs and results may not be generalizable to other settings, such as in other countries of the European Union or the United States. Finally, although we cannot know what the answers of the nonrespondents would be, given the very high response rate, our results probably are not confounded by this.

Our results cast light on other important aspects of residency training as, along with gaining clinical experience and improving practical skills, residents are in need of good teachers and mentors, good support from colleagues, a manageable workload, and a working environment with fewer emotional demands. Autonomy is crucial, as well as having a good balance between home and work demands. Interestingly, the

In total, 21 residents (18.1%) were found to experience burnout. Table 2 shows the characteristics of those with and without burnout syndrome. There were no statistically significant differences regarding demographic and work-related characteristics between the 2 groups. However, regarding the JD-R characteristics, residents with burnout had less support from their supervisor, experienced increased workload, had experienced conflicts in the interface between familial and professional life, had less autonomy at work, and had fewer professional development chances.

The following independent variables were entered into the multivariate logistic regression model: sex, age, supervisor support, work–home demands interface, autonomy, and opportunities for professional development. The model χ² value indicated that there was a statistically significant overall relationship between the dependent variable and the set of independent variables (χ² = 29.27, df = 6, p < 0.001). The χ² value associated with the Hosmer-Lemeshow test (χ² = 6.17, df = 8, p = 0.628) indicated a good overall model fit. The Nagelkerke R² was equal to 36.6%. According to the Wald criterion, only the unstandardized coefficient for opportunities for professional development (β = −0.338) was found to reach statistical significance (p = 0.012). Each increased point for opportunities for professional development was associated with a 28.7% decrease in the odds of burnout.

### Table 2 Characteristics of neurology residents with and without burnout

<table>
<thead>
<tr>
<th></th>
<th>Residents with burnout (n = 21)</th>
<th>Residents without burnout (n = 95)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>34.6 (4.5)</td>
<td>34.5 (3.4)</td>
<td>0.988</td>
</tr>
<tr>
<td>Male sex</td>
<td>13 (61.9)</td>
<td>39 (41.1)</td>
<td>0.082</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td>0.704</td>
</tr>
<tr>
<td>Single</td>
<td>14 (66.7)</td>
<td>55 (57.9)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>9 (33.3)</td>
<td>39 (41.1)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>0 (0.0)</td>
<td>1 (1.1)</td>
<td></td>
</tr>
<tr>
<td><strong>Work-related characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months remaining to complete training</td>
<td>19.3 (10.7)</td>
<td>17.7 (10.8)</td>
<td>0.525</td>
</tr>
<tr>
<td>Working hours per day (not including on-call duties)</td>
<td>7.3 (1.3)</td>
<td>7.1 (1.0)</td>
<td>0.398</td>
</tr>
<tr>
<td>On calls per month</td>
<td>4.6 (2.4)</td>
<td>4.7 (1.5)</td>
<td>0.851</td>
</tr>
<tr>
<td>Days off per month</td>
<td>1.8 (1.5)</td>
<td>2.5 (1.6)</td>
<td>0.057</td>
</tr>
<tr>
<td>EWTD violated</td>
<td>5 (23.8)</td>
<td>9 (9.5)</td>
<td>0.068</td>
</tr>
<tr>
<td><strong>Job demands and resources</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>11.5 (2.7)</td>
<td>12.3 (2.5)</td>
<td>0.163</td>
</tr>
<tr>
<td>Supervisor support</td>
<td>12.5 (5.1)</td>
<td>15.3 (4.6)</td>
<td>0.014c</td>
</tr>
<tr>
<td>Workload</td>
<td>15.1 (5.2)</td>
<td>14.7 (3.0)</td>
<td>0.663</td>
</tr>
<tr>
<td>Intellectual demands</td>
<td>11.6 (2.8)</td>
<td>11.8 (2.2)</td>
<td>0.762</td>
</tr>
<tr>
<td>Emotional demands</td>
<td>22.3 (4.3)</td>
<td>20.8 (3.8)</td>
<td>0.113</td>
</tr>
<tr>
<td>Work-home demands conflict</td>
<td>12.6 (3.8)</td>
<td>9.5 (2.7)</td>
<td>0.007b</td>
</tr>
<tr>
<td>Autonomy</td>
<td>7.4 (2.2)</td>
<td>9.6 (2.7)</td>
<td>0.001b</td>
</tr>
<tr>
<td>Opportunities for professional development</td>
<td>7.6 (2.3)</td>
<td>10.7 (2.9)</td>
<td>&lt;0.001c</td>
</tr>
</tbody>
</table>

Abbreviation: EWTD = European Working Time Directive. Noncontinuous variables are given as percentages. Continuous are presented as means with their corresponding SD.

*a p < 0.05.

*b p < 0.01.

*c p < 0.001.
multivariate analysis showed that opportunities for professional development remained the most significant determinant of burnout. Such opportunities may include research opportunities, chances of attending educational seminars or conferences, and active involvement in teaching medical students or more junior doctors.

Preventing burnout is crucial not only for health service employees but also for health service users. Regional health care systems should avail educators and program directors with the provisions needed to facilitate burnout prevention, initially by providing further opportunities for residents’ professional development.

AUTHOR CONTRIBUTIONS

Panagiotis Zis: drafting/revising the manuscript, study concept and design, data collection, statistical analysis, accepts responsibility for conduct of research and final approval. Artemios K. Artemiadis, Maria Lykouri, Sophia Xionou, Andromachi Roussopoulou, Ermioni Papageorgiou, Eleni Bakola: drafting/revising the manuscript, data collection, accepts responsibility for conduct of research and final approval. Fotios Anagnostopoulos: drafting/revising the manuscript, study concept and design, accepts responsibility for conduct of research and final approval.

ACKNOWLEDGMENT

The authors thank Dr. Serafeim Katsavos, Dr. Panagiotis Ilissiopoulos, and Dr. Ioannis Stavropoulos for contribution to data collection; and the study participants.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

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

REFERENCES

Teaching NeuroImages

Teaching NeuroImages are interesting, previously unpublished photomicrographs, patient photographs, neuroradiologic images, or other pictorial material. They are clear examples of established observations intended for the trainee audience. Educational videos may also be submitted under this category (Teaching Video NeuroImages). Teaching NeuroImages and Teaching Video NeuroImages now feature accompanying ‘Teaching Slides.’ These slides are available online with the article as a teaching tool for trainees and program directors.
Teaching NeuroImages: The lentiform fork sign
An MRI pattern of metformin-associated encephalopathy

Gustavo C. Fernandes, MD
Tássia Koltermann, MD
Lillian Campos, MD
Leonardo Vedolin, MD, PhD
Carlos R.M. Rieder, MD, PhD

Correspondence to
Dr. Fernandes:
gcostafernandes@yahoo.com

(A) Axial noncontrast CT shows bilateral hypodensities in the basal ganglia. (B) Brain MRI reveals a pattern of vasogenic edema with T2/fluid-attenuated inversion recovery hyperintensity in the basal ganglia compatible with the lentiform fork sign.

A 63-year-old woman with type 2 diabetes mellitus on hemodialysis presented with subacute onset of slurred speech and difficulty walking after 1 week of inadvertent metformin use.

On examination, she had a wide-based gait, symmetric upper limb rigidity, bradykinesia, and slurred speech.

Brain MRI revealed a pattern of vasogenic edema with T2/fluid-attenuated inversion recovery hyperintensity in the basal ganglia compatible with the lentiform fork sign (1).

Basal ganglia pathology has been described on the setting of metabolic acidosis and metformin use in hemodialysis patients, resulting in a parkinsonian syndrome (2).

STUDY FUNDING
No targeted funding reported.

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

REFERENCES
Teaching Video NeuroImages

Teaching Video NeuroImages have the same requirements as Teaching NeuroImages except they are accompanied by a video. Videos should portray interesting, previously unpublished photomicrographs, patient photographs, neuroradiologic images, or other pictorial material. They are clear examples of established observations intended for the trainee audience. Educational videos may also be submitted under this category (Teaching Video NeuroImages).

Teaching NeuroImages and Teaching Video NeuroImages now feature accompanying ‘Teaching Slides.’ These slides are available online with the article as a teaching tool for trainees and program directors.
Feeding dystonia in chorea-acanthocytosis

A 39-year-old man was evaluated for personality change, involuntary movements, and eating difficulties. Examination demonstrated feeding dystonia, dysarthria, limb dystonia, and chorea (video on the Neurology® Web site at Neurology.org). Transaminases and creatine kinase levels were elevated. Additional investigation revealed acanthocytes on blood smear, myopathy, and caudate nucleus atrophy (figures 1, 2, e-1, and e-2). Western blot revealed absent chorein, and a genetic test found him to be compound heterozygote for novel VPS13A gene mutations (c.266dupT and deletion of exons 52, 53, 55, and 58), establishing a diagnosis of chorea-acanthocytosis. He was treated with botulinum toxin injections in genioglossus, which significantly improved eating and speaking.

ACKNOWLEDGMENT
Western blot analysis for chorein was performed by G. Kwiatkowski and Dr. Benedikt Bader with the financial support of the Advocacy for Neuroacanthocytosis Patients and of the ERA-net E-Rare consortium EMINA (European Multidisciplinary Initiative on Neuroacanthocytosis; BMBF 01GM1003) in the labs of Profs. Hans Kretzschmar/Armin Giese (Neuropathology) and Adrian Danek (Neurology) at Ludwig-Maximilians-Universität, Munich, Germany.

STUDY FUNDING
Stockholm County Council.

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

REFERENCE
Thanks to Wolters Kluwer

The Neurology Resident & Fellow Editors would like to acknowledge Wolters Kluwer for their support of the RFS Highlights booklet including producing print version; establishing online, mobile, and iPad presence; and providing flash drives for trainees at the Annual Meeting.