Annual Highlights of the Resident & Fellow Section: 2015

A Representative Collection of Previously Published Articles

Meet the Resident & Fellow Editors of Neurology

And learn how you can contribute to the journal at the Residents & Fellows Career Forum and Reception

Monday, April 20, 2015, 7:30 p.m.–9:00 p.m.

Marriott Marquis Washington, Marquis Ballroom
Announcement

Neurology® Resident & Fellow Section Writing Award
The winners of the 2015 Award are:

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

The winners will be honored at the 2015 AAN awards luncheon. See page 15 of this Highlights booklet for the award-winning article.

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 2016 and will be awarded for a paper published in 2015.

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

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.
January 7, 2014 82: e5-e7

2013 Award Winner
Daniel R. Gold, DO, and Stephen G. Reich, MD
October 23, 2012 79: e146-e152

2012 Award Winner
Christina B. Pham, MD, Johannes R. Kratz, MD, Angie C. Jelin, MD, and Amy Gelfand, MD
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
# Table of Contents

1. *Neurology Resident & Fellow Section Editorial Team*

2. **The Neurology Resident and Fellow Section: The Second Decade Begins!**
   Mitchell S.V. Elkind, John J. Millichap, Kathleen Pieper

3. **Top 10 Ways for Program Directors to Use the Neurology Resident & Fellow Section (RFS)**
   S. Lapalme-Remis, S. Stern-Nezer, V.S.S. Wong, and J.J. Millichap

4. **Where Are They Now?**
   Past RFS Editorial Team Member Updates

5. **Child Neurology**
   8. *Tick paralysis: A diagnosis not to miss*  
      S.L. Chagnon, M. Naik, and H. Abdel-Hamid  
      | February 11, 2014; 82: e46-e50
   11. *Brachial plexus birth injury: What every neurologist needs to know*  
      C.B. Pham, J.R. Kratz, A.C. Jelin, and A.A. Gelfand  
      | August 16, 2011; 77: 695-697

6. **Clinical Reasoning**
   15. *An unusual cause of transverse myelitis?*  
      P. Bhargava and R.J. Elble  
      | February 11, 2014; 82: e46-e50

7. **Education Research**
   25. *Case logs in the assessment of medical students in the neurology out patient clinic*  
      D.V. Albert, J.R. Brorson, C. Amidei, and R.V. Lukas  
      | April 22, 2014; 82: e138-141

8. **Emerging Subspecialties in Neurology**
   34. *Neuropalliative care*  
      M.T. Robinson and K.M. Barrett  
      | May 27, 2014; 82: e180-e182
   37. *Fellowship in experimental therapeutics of neurologic disease*  
      J.M. Statland, R.C. Griggs, and E.F. Augustine  
      | September 25, 2012; 79: e106-e108

9. **International Issues**
   41. *Acute ischemic stroke: An international experience*  
      M. Colling, V-A Lioutas, and V. Krishnan  
      | November 4, 2014; 83: e174-e176
   44. *International Education Issues: Neurology and poverty*  
      F.J. Mateen  
      | October 23, 2007; 69: 1724-1726

10. **Neurology Journal Club**
    48. *Comparison of symptomatic and a symptomatic persons with Alzheimer disease neuropathology*  
        J.R. Brosch and B.R. Matthews  
        | March 4, 2014; 82: e76-e78

11. **Opinion & Special Articles**
    51. *Early stroke risk and ABCD2 score performance in tissue vs time-defined TIA*  
        J.E. Fugate and A.A. Rabinstein  
        | March 20, 2012; 78: e77-e79

12. **Residency Training**
    78. *The role of neurocritical care in resident education*  
        I.R.F. Da Silva and J.A. Gomes  
        | January 29, 2013; 80: e51-53

13. **Right Brain**
    86. *Humor completes the neurologic exam*  
        P. Bhargava  
        | January 21, 2014; 82: e21-e22

14. **Teaching NeuroImages & Teaching Video NeuroImages**
    91. *Brain mass with hilar adenopathy: The importance of histologic diagnosis*  
        J.T. Jordan, H-S Yang, and S.R. Plotkin  
        | May 6, 2014; 82: e161-e162

15. **E-Pearls of the Week**
    97. *Parechovirus and Neurologic Disease*  
        A. Numis  
        | June 20, 2014

16. **Mystery Case**
    54. *Eyelid myoclonia with absences in an adult patient*  
        Y. Hannawi, S.S. Satpute, and A. Maheshwari  
        | February 25, 2014; 82: e63-e64

17. **Mystery Case**
    57. *A young boy with myoclonic jerks*  
        C. Musleh, L. Marcuse, and J.J. Millichap  
        | October 29, 2013; 81: e130-e134

18. **Mystery Case**
    65. *A guide from fellowship to faculty: Nietzsche and the academic neurologist*  
        S.T. Carmichael  
        | October 2, 2012; 79: e116-e119

19. **Mystery Case**
    69. *Rapidly progressive dementia: Prions or immunomediated?*  
        | April 29, 2014; 82: e149-e152

20. **Mystery Case**
    73. *Trigeminal autonomic cephalalgias*  
        C.A. Whyte and S.J. Tepper  
        | March 16, 2010; 74: e40-e42

21. **Mystery Case**
    77. *Developing a program of quality and safety to train resident neurologists for the future*  
        S.A. Josephson and J.W. Engstrom  
        | February 21, 2012; 78: 602-605

22. **Mystery Case**
    88. *The blind spot*  
        C.B. Pham  
        | August 16, 2011; 77: 698-699

23. **Mystery Case**
    90. *Brain mass with hilar adenopathy: The importance of histologic diagnosis*  
        J.T. Jordan, H-S Yang, and S.R. Plotkin  
        | May 6, 2014; 82: e161-e162

24. **Mystery Case**
    93. *A tasteless lesion*  
        | July 11, 2006; 67: E1

25. **Mystery Case**
    94. *Semiaology and localization of ballistic movements*  
        H. Gonzalez-Usigli and A.J. Espay  
        | July 22, 2014; 83: e56-57

26. **Mystery Case**
    96. *Complicated scapular winging*  
        M. Monforte, E. Ricci, E. Iannaccone and G Tasca  
        | September 17, 2013; 81: e95

27. **Mystery Case**
    97. *HINT of Stroke*  
        R. Strowd  
        | July 8, 2013

*Winner of the 2015 R&F Writing Award*
John Millichap is a pediatric epileptologist in the Division of Neurology Clinical Outcomes Research and Population Sciences (NeuroCORPS), and fellowships director for the Neurology Department. His research is focused on inflammatory and infectious biomarkers in stroke risk prediction, as well as acute stroke therapy. Dr. Millichap is a principal or co-investigator in several federally-funded research projects related to stroke risk and outcomes, including: the NeuSTART (Neuroprotection with Statin Therapy for Acute Recovery Trial), a clinical trial evaluating short-term high-dose statin therapy in acute stroke; Levels of Inflammatory Markers in the Treatment of Stroke (LUMIRTS), a multi-center biomarker study among lacunar stroke patients; and the Northern Manhattan Stroke Study, a prospective cohort study of stroke risk factors. He is former neurology residency program director at Columbia University, and a fellow of the American Academy of Neurology and the American Heart Association. He has mentored several residents and fellows in neurology and clinical research.

Deputy Section Editor

John J. Millichap, MD, FAAP
John Millichap is a pediatric epileptologist in the Comprehensive Epilepsy Center at Ann & Robert H. Lurie Children’s Hospital of Chicago and an assistant professor of pediatrics and neurology at Northwestern University Feinberg School of Medicine. His education includes a bachelor of arts from Northwestern University and a medical doctorate from American University of the Caribbean School of Medicine. Dr. Millichap trained in Pediatrics at the Brody School of Medicine at East Carolina University prior to child neurology and clinical neurophysiology/pediatric epilepsy fellowships at Northwestern University. Current clinical practice utilizes a multidisciplinary team approach to the diagnosis and treatment of epilepsy and comorbidities. As a member of the academic faculty, he is involved in the education of trainees and grant funded clinical research concerning epileptic encephalopathies. Dr. Millichap is an avid writer himself and enjoys encouraging resident and fellow contributions to the medical literature.

Editor

Mitchell S.V. Elkind, MD, MS, FAAN
Dr. Elkind graduated from Harvard Medical School, and completed neurology residency at Massachusetts General Hospital. He obtained a master’s degree in epidemiology from Columbia University during his stroke fellowship. Currently, Dr. Elkind is a professor of neurology and epidemiology at Columbia University, head of the Division of Neurology Clinical Outcomes Research and Population Sciences (NeuroCORPS), and fellowships director for the Neurology Department. His research is focused on inflammatory and infectious biomarkers in stroke risk prediction, as well as acute stroke therapy. Dr. Elkind is a principal or co-investigator in several federally-funded research projects related to stroke risk and outcomes, including: the NeuSTART (Neuroprotection with Statin Therapy for Acute Recovery Trial), a clinical trial evaluating short-term high-dose statin therapy in acute stroke; Levels of Inflammatory Markers in the Treatment of Stroke (LUMIRTS), a multi-center biomarker study among lacunar stroke patients; and the Northern Manhattan Stroke Study, a prospective cohort study of stroke risk factors. He is former neurology residency program director at Columbia University, and a fellow of the American Academy of Neurology and the American Heart Association. He has mentored several residents and fellows in neurology and clinical research.

Editorial Team, Resident & Fellow Section

James Addington, MD
James Addington is an adult neurology resident at the University of Virginia. He graduated from Miami University in Oxford, OH, with a degree in zoology and neurosciences prior to completing his medical degree at Indiana University. His academic interests include neuromuscular medicine, more specifically the use of translational research and clinical trials. As well, he has a strong interest in health care policy, cost-effective utilization and medical education.

Luca Bartolini, MD
Luca Bartolini is a child neurology fellow at Children’s National Health System in Washington, DC. He graduated from the School of Medicine of the University of Padua, Italy, and completed his pediatric training first at the University of Padua and then at Children’s National. He intends to obtain subspeciality training in epilepsy. As part of his basic neuroscience pathway to board certification, he will investigate the role of viral infections in the pathophysiology of epilepsy at the Viral Immunology Section of the NIH.

Miya Bernson-Leung, MD
Miya Bernson-Leung received her undergraduate degree from Harvard College and her medical degree from Harvard Medical School. She is now training in child neurology at Boston Children’s Hospital following her pediatrics residency in the Boston Combined Residency in Pediatrics. She intends to pursue subspeciality training in pediatric stroke followed by an academic child neurology practice with a focus on medical education at the student and resident level.

Joseph Cahill, MD
Joseph Cahill is chief neurology resident at the University of Wisconsin. He attended medical school at the Universitad Autonoma de Guadalajara in Guadalajara, Mexico, after serving eight years as an active duty hospital corpsman in the US Navy. He is also a screenwriter whose credits include, Manipulating Life, and La Solitude both of which have screen in film festivals in the US and abroad.

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 Battten’s Disease.

Carla Francisco, MD
Carla Francisco is a child neurology fellow at Children’s Hospital Los Angeles. She obtained her bachelor’s degree in chemistry from Pomona College in Claremont, CA. She graduated from the Keck School of Medicine of the USC and completed her pediatric training at Children’s Hospital Los Angeles.

Aravind Ganesh, MD
Aravind Ganesh is a neurology resident at the University of Calgary, where he completed his MD training in 2012. He was awarded a Rhodes scholarship in 2014, through which he is pursuing a DPhil in Clinical Neurosciences while serving as a Clinical Research Fellow at the University of Oxford’s Centre for Prevention of Stroke and Dementia. His research interests and publications focus on stroke, MS, neuropsychiatric disorders, and neuroscience history. He is passionate about medical education and is a public health and policy advocate.

Cliff Hampton, MD
Cliff Hampton is a neurology resident at the University of Colorado in Denver. He graduated from Weber State University in Ogden, Utah with a degree in Spanish Language and obtained his medical degree from Baylor College of Medicine in Houston, Texas. In addition general neurology, he is also interested in bioethics and its relationship to the field of neurology.

Andrea Harriott, MD, PhD
Andrea Harriott is a neurology resident at Mayo Clinic in Jacksonville, FL. She earned a Bachelor of Science degree from Morgan State University. She earned her MD and PhD degrees from University of Maryland in Baltimore, MD. Recent research endeavors include investigating associations between genetic variants, migraine, and stroke risk. She continues to pursue translational and basic science research with academic interests in headache and stroke.

Jonathan T. Kleinman, MD
Jonathan T. Kleinman grew up in Minnesota where all the women are strong, all the men are good-looking, and all the children are above average. He studied cellular and molecular neuroscience while attending Johns Hopkins. After college he stayed to do research with the department of neuroscience, studying aphasia and spatial neglect. He went to medical school at Stanford. Jon hopes to pursue a career in academic neurology.

Shaheen E. Lakhani, MD, PhD, MED, MS
Shaheen Lakhani is a Clinical Instructor of Medicine at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve. After graduating from medical school at the Technion Israel Institute of Technology, he completed neurology residency training at the Cleveland Clinic and is now a Clinical Fellow in Anesthesiology (Pain Medicine) at Massachusetts General Hospital, Harvard Medical School.

Samuel Lapalme-Remis, MD, MA
Samuel Lapalme-Remis is a fourth-year resident in adult neurology at the University of Ottawa. He completed both his undergraduate studies and his MD at McGill University. Prior to medical school, he worked in Japan for several years while completing an MA in Japanese language and society from the University of Sheffield. His academic interests include epilepsy, medical education, qualitative research, and medicine in Japan.
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Institution</th>
<th>Current Position</th>
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</thead>
<tbody>
<tr>
<td>Matthew R. Lincoln, MD, DPhil</td>
<td>Neurology Resident</td>
<td>Stanford University</td>
<td>Resident at the University of Toronto.</td>
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<tr>
<td>Kristen Lindgren, MD, PhD</td>
<td>Neurology Resident</td>
<td>Massachusetts General Hospital (MGH)</td>
<td>Resident at the University of Toronto.</td>
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<td>Khaled Moussawi, MD, PhD</td>
<td>Neurology Resident</td>
<td>Medical University of South Carolina</td>
<td>Adult Neurology Resident at the University of Toronto.</td>
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<td>Adam Numis</td>
<td>Neurology Fellow</td>
<td>University of California, San Francisco</td>
<td>Child Neurology Fellow at the University of California.</td>
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<td>Craig Press, MD, PhD</td>
<td>Neurology Resident</td>
<td>University of Colorado Denver</td>
<td>Child Neurology Resident at the University of Colorado.</td>
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<td>Andrew Sas, MD, PhD</td>
<td>Neurology Resident</td>
<td>University of Michigan</td>
<td>Neurology Resident at the University of Michigan.</td>
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<td>Andrew Schepmyer, MD</td>
<td>Neurology Fellow</td>
<td>University of British Columbia</td>
<td>Neurology Fellow at the University of British Columbia.</td>
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<td>Raphael Schneider, MD</td>
<td>Neurology Resident</td>
<td>University at Buffalo in 2012</td>
<td>Neurology Resident at the University of Buffalo in 2012.</td>
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<td>Sarah Wesley, MD MPH</td>
<td>Neurology Fellow</td>
<td>Lake Forest College in 2007</td>
<td>Neurology Resident at Lake Forest College.</td>
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<tr>
<td>Michael White, MD</td>
<td>Neurology Fellow</td>
<td>Lake Forest College in 2007</td>
<td>Neurology Resident at Lake Forest College.</td>
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Sara Stern-Nezer graduated from Columbia University and earned her MD/MPH at Stanford University and UC Berkeley. While obtaining her masters, she worked on diverse global health projects from the effects of indoor fossil fuels on pulmonary health in developing countries. She started a site for an RCT in Zambia looking at low-cost interventions to reduce maternal mortality. She is now an adult neurology resident at Stanford University.

Matthew Lincoln is a third-year neurology resident at the University of Toronto. He is a graduate of Harvard College and earned his MD at the University of Toronto. 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.

Kristen Lindgren is a child neurology resident at Massachusetts General Hospital (MGH). She obtained her B.A. from Wesleyan University and then earned her MD and PhD degrees from Boston University School of Medicine. She completed her pediatrics training at MGH. Her clinical and research interests include autism spectrum disorder and other related developmental disorders.

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 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.

Craig Press is currently a child neurology resident at the University of Colorado Denver. He studied biomedical engineering at Northwestern University while focusing his research on neurodegenerative diseases and gene therapy. He received his MD/PhD from Washington University in St. Louis where he studied the mechanisms of axonal. His interests focus on pediatric neurocritical care, epilepsy, and traumatic brain injury.

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.

Andrew Schepmyer completed his bachelor of science degree at McMaster University in Hamilton, Ontario, in 2007, and then went on to earn his medical degree at the University of Toronto in 2011. He is currently in the second year of his adult neurology residency at the University of British Columbia in Vancouver. His academic interests include autoimmune and infectious diseases of the nervous system as well as medical education.

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.

Sara 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 and an MPH from Dartmouth College’s Institute for health policy and clinical practice, focusing on exposure risk analysis in epilepsy and autism. Currently, she is a neurology resident at Mount Sinai Beth Israel in New York City and has contributed to a number of educational and research publications, including first aid for the USMLE. She plans to pursue a fellowship in neuroimmunology and multiple sclerosis.

Sarah 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 and an MPH from Dartmouth College’s Institute for health policy and clinical practice, focusing on exposure risk analysis in epilepsy and autism. Currently, she is a neurology resident at Mount Sinai Beth Israel in New York City and has contributed to a number of educational and research publications, including first aid for the USMLE. She plans to pursue a fellowship in neuroimmunology and multiple sclerosis.

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The *Neurology* Resident & Fellow Section: The Second Decade Begins!

Mitchell S.V. Elkind, John J. Millichap, Kathleen Pieper

In 2004, Berch Griggs, then the editor-in-chief of *Neurology*, and Karen Johnston, associate editor, launched the Resident & Fellow Page as a forum for trainees and educators to publish articles on topics relevant to residency and fellowship. Articles in this experimental page included clinical reviews and education research projects, as well as commentaries on practice, ethics, teaching, history, and international training experiences. By 2014, ten years later, the “Page” had become a “Section,” with articles appearing weekly, projects like Podcasts and the Writing Award, and a growing team of editorial team members from around the world. In this decade, *Neurology* also enhanced reader access by adding a mobile version and an iPad® app. In 2015, we begin our second decade of the Resident & Fellow Section with a number of new initiatives and projects underway.

The Resident & Fellow Section (RFS) is trainee-run: A nationally representative team of 15-20 residents and fellows, each of whom serves three years, has responsibility for reviewing, editing, and publishing articles. Residents are now selected annually, through a competitive process that attracts dozens of applicants from the US and abroad. 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. Readers can learn about past and current team members, and the role of this experience in their careers, in this Highlights booklet.

Over the years, editorial team members have also introduced several different subsections, many represented by the articles in this booklet. These include articles related to clinical neurological education, such as those in the Clinical Reasoning, Pearls and Oy-sters, Child Neurology, and Teaching NeuroImages (including both static images and videos) sections; those related to residency training, such as the International Issues and Education Research and Initiatives sections; and articles related to career issues, exemplified by those in the Emerging Subspecialties in Neurology section. The Right Brain section includes creative writing. More recent additions include Mystery Cases and Book and Media Reviews. Descriptions of these subsections appear before each sample article.

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), and the Journal Club (2011). Our 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.

What will the next decade of the RFS bring? It is too soon to say for sure, but we plan to start by introducing a course on writing case reports, using the new CAse REport (CARE) writing guidelines, at the 2015 AAN Annual Meeting. And our next big project, we hope, will be to compile some of the finest and most interesting Clinical Reasoning cases from among the more than 130 published during the first decade into an educational resource for trainees and program directors. After that, our endeavors will be limited only by the imagination and efforts of our team members and others interested in neurology education.

*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 Mitchell Elkind, John Millichap, or Kathy Pieper at kpieper@neurology.org.

We hope you enjoy this special Tenth Anniversary Edition of the Highlights of the RFS!

Mitchell S. V. Elkind, MD, MS, FAAN, Associate Editor, Resident and Fellow Section

John J. Millichap, 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 (RFS)

Samuel Lapalme-Remis, Sara Stern-Nezer, Victoria S.S. Wong, John J. Millichap

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

1. Every Teaching Neurolmage has a supplemental PowerPoint slide set available for download from the Neurology® website that may be used for group presentations.

2. A Clinical Reasoning article can easily be the basis for a one-hour educational resident conference. The piece is formatted for teaching and has sections with questions for consideration.

3. Journal Club articles provide critical appraisals of articles published in Neurology. 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 may provide ideas for what to purchase with book funds. In addition to traditional texts, the RFS reviews neurology apps and other electronic media.

6. The Right Brain subsection allows you to exercise your “write” brain by composing your neurological narratives and submitting them.

7. The Education Research subsection reports quality research on educational topics including surveys of program directors and residents, as well as studies about educational interventions and resident evaluation.

8. Scholarly activity among residents and fellows can be promoted 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, send us manuscript submissions, and apply for a position on our editorial team during our annual recruitment!
Where Are the RFS Team Members Now?

Launched in 2004, the RFS has experienced a decade of success due to the current and past editorial teams. Then Editor-in-Chief, Robert Griggs, and the founding Editor, Karen Johnston, established an editorial team of four resident members: Beau Ances, David Gill, Dan Larriviere, and Michele Yang. Their primary responsibility was to establish the criteria for the submission categories, encourage submissions, and make it known to their program directors and peers that the RFS had launched! The first year, the RFS received 14 manuscripts and published 12 articles. Since 2005, we have received 2,252 manuscripts and published 896.

Editorial team members served three-year terms beginning in 2007 under the leadership of Mitch Elkind. Support and growth of the section continued under Neurology Editor-in-Chief Dr. Robert Gross, appointed in 2009. John Millichap joined the RFS leadership as Deputy Editor in 2011. We thank the following RFS past team members: Megan Alcauskas, James Berry, Audrey Brumback, Rajani Ruth Caesar, Stacey Clardy, Jennifer Fugate, Amy Gelfand, Daniel Goldenholz, James Gregory, Fabio M. Iwamoto, Shafali Jeste, Chafic Karam, Sheng-Han Kuo, Irfan Lalani, Farrah Mateen, Dragos Nita, Christopher Nolte, Ryan Overman, James Park, Shanna Patterson, Sashank Prasad, Peter Pressman, Keith Ridel, Sarah Song, Roy Strowd, Christine Ulane, James Watson, Victoria Wong, and Holly Yancy.

Where are they now?
We surveyed our past RFS editorial team members about their experiences since serving on the RFS.

What best describes their current practice setting?
The majority (70 percent) of the respondents are in academic institutions in research; the remainder are in academic institution settings in a clinical position, and one member is now in private practice.

What other activities are they involved in?
Of the respondents, 80 percent are involved in medical student and/or resident student education. Fifty percent have also pursued some type of medical advocacy (work with the AAN, patient advocacy) and 10 percent were involved in online educational vehicles (blogs, educational podcasts, or forums).

What is their current focus or subspecialty?
We found that the highest numbers fell in general neurology and pediatric neurology. We had slightly lower numbers go into the fields of neuroimmunology and behavioral/cognitive disorders. Fewer former members pursued subspecialties of infectious disease, vascular, epilepsy, movement disorders, or neuromuscular disease.

What did they learn from the experience?
I am thankful that Neurology included this section in the journal. I think it really gives students, residents, and fellows an outlet for expressing themselves that few other journals provide.

—Beau Ances, MD, Associate Professor in the Department of Neurology and Neurosciences, Washington University, Editorial Team Member, 2003–2006

Reviewing articles further developed my critical thinking skills. Participation in the regularly scheduled conference calls and brainstorming about new ideas for education and segments within the section solidified my interest in pursuing a career in neurology focusing on graduate medical education.

—Christina Ulane, MD, PhD, Assistant Professor of Neurology, Columbia University, Editorial Team Member, 2009–2012

The RFS was my first involvement with any part of the AAN organization apart from just being a member. Now I am transitioning to advocacy work on behalf of the AAN and neurology education through the Palatucci Advocacy Leadership Forum. The RFS was great preparation for involvement outside my home institution.

—Anonymous

As an academic child neurologist, I have to review for many high-impact journals and also am submitting manuscripts to high-impact journals. The RFS provided me with a valuable introduction to the editorial process and helped me to develop the skills necessary to both review and write manuscripts for scientific audiences.

—Shafali Jeste, MD, Assistant Professor in Psychiatry and Neurology, UCLA, Editorial Team Member, 2007–2010

It was a terrific education on the workings of the editorial process. It also reinforced my notion that I wanted to remain in academics. I also met many fantastic colleagues.

—Stacey Clardy, MD, Assistant Professor of Neurology, University of Utah, Editorial Team Member, 2009–2012

It got me thinking about the ways in which I could get involved in editing and writing as a neurologist, something I thought I wouldn’t necessarily be able to do. It was a way to think with a different part of my brain (as opposed to the majority of my brain, which was focused on getting through residency and fellowship!). I also think that being on the Resident & Fellow Section gave me a lot of credibility in terms of my editing experience. Not shortly after my stint on the section ended, I worked as the advocacy editor for the AAN website, a job that I might not have gotten
(or even offered) if it hadn’t been for my prior experience. As a result of working on the website, I was recently offered a spot on the editorial board of *Neurology Now*, which I am just starting. I also serve on the Government Relations Committee of the AAN, through which I have been able to help write and edit multiple position and legislative statements, which has also been really interesting and a lot of fun.

—Sarah Song, MD, MPH, Assistant Professor of Neurology, Rush University, Editorial Team Member, 2008–2011

The relationships that I developed over the three years with the section have endured and continued to open important doors for my academic and scholastic advancement. In addition, the skills I developed as an editorial member have assisted me greatly in developing the comfort and expertise necessary to continue to review and write scholastically.

—Roy Strowd, MD, Assistant Professor of Neurology, Johns Hopkins School of Medicine, Editorial Team Member, 2011–2014

Immediately post-residency, I stayed in academic medicine and was very involved in education, as clerkship director and assistant residency director of my institution for several years. This was partially inspired by the confidence I gained from being a part of the RFS where I felt like I had something to contribute.

—Megan Alcauskas, MD, Editorial Team Member, 2006–2009

It allowed me the opportunity to work closely with the editorial staff, meet residents and fellows at other institutions, and leverage the amazing forum that *Neurology* is for practicing neurologists around the world.

—Farrah Mateen, MD, PhD, Assistant Professor of Neurology, Harvard Medical School, Editorial team Member 2006–2009

Any advice to trainees?

Find what truly excites you—whether it be a scientific and research-based career (possibly sparked by review for the R&F Section!) or a focus on education or patient care. Participation on the R&F Section editorial board provides a great way to expose one to a wider variety of neurological topics, but also offers a fantastic opportunity to get involved with education.

—Christina Ulane, MD, PhD, Assistant Professor of Neurology, Columbia University, Editorial Team Member, 2009–2012

Identify and build mentoring relationships—more than one, as early as possible.

1. Choose a good mentor who can guide you not only on specific career choices but also on the work-life balance.
2. Do not say yes to everything that is asked of you, learn to prioritize and use your mentor to help you decide what to accept.

3. For those in academia, make both writing and reading a priority and dedicate time to both at least once weekly.

4. Choose the path that allows you to do what you actually love, not what you think you should love. Success only comes when you are working towards a goal that is meaningful and fulfilling for you.

—Shafali Jeste, MD, Assistant Professor in Psychiatry and Neurology, UCLA, Editorial Team Member, 2007–2010

Career planning can be one of the most challenging aspects of residency and fellowship. Mentors are always important and the RFS is a good way to expand mentorship nationally… I would also encourage junior members to work hard to engage their local faculty in the section. I found this to be a very rewarding way not only to spark interest in the section but to connect with mentors, writing partners, and collaborators who had an interest in helping support my career but with whom I had not previously connected prior to reaching out about these opportunities.

—Roy Strowd, MD, Assistant Professor of Neurology, Johns Hopkins School of Medicine

Spend your time as a trainee figuring out what your primary career goal is (e.g., subspecialty/fellowship, practice setting, practice location, research grants) and work towards it.

—Victoria S.S. Wong, MD, Assistant Professor of Neurology, Oregon Health and Science University, Editorial team Member, 2009–2012

Find what you are passionate about, and focus on that.

—Daniel Goldenholz, MD, PhD, Clinical Epilepsy Fellow, NIH Editorial Team Member, 2010-2014

Actively seek mentors and set up recurring meetings with them to review specific aspects of your professional development: Publications, grant funding, scientific contributions, clinical expertise, teaching, talks, outreach, salary structure, one year plan, five year plan.

—Audrey Brumback, MD, PhD, Assistant Professor of Neurology and Pediatrics, UCSF, Editorial Team Member, 2010–2014

Writing writing writing and publishing!

—Sheng-Han Kuo, MD, PhD, Assistant Professor of Neurology, Columbia University, Editorial Team Member, 2008–2011
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: Tick paralysis
A diagnosis not to miss

Sarah L. Chagnon, MD
Monica Naik, MD
Hoda Abdel-Hamid, MD

A 4-year-old girl presented to our tertiary care hospital with a complaint of lower extremity weakness and unsteady gait for 2 days. She was able to pull herself to stand but could not stand unsupported. She had no sensory symptoms or pain. She did not complain of any weakness in her arms, trunk, face, or neck. She had no bowel or bladder incontinence or retention. On presentation to the emergency department, she had minimal antigravity strength of the lower extremities but normal strength elsewhere. In addition, she was areflexic in both lower extremities and had a wide-based, unsteady gait but no appendicular dysmetria or titubation. Sensory examination was normal.

After consultation by the neurology service, MRI of the brain and total spine were completed and a plan was made for subsequent lumbar puncture. Lyme disease antibodies were drawn because of exposure to a wooded area in West Virginia; these were negative. MRI of the spine showed syringomyelia extending from T5 to T8 and an extramedullary, intradural cystic lesion dorsal to the spinal cord from T1 to T4, which was believed to be consistent with an arachnoid cyst. Due to this unexpected finding, the neurosurgical service was consulted, who believed that this cyst and the associated syrinx were the source of her paralysis. The following day, she was taken to the operating room for fenestration. Subsequent to the fenestration, repeat imaging showed resolution of syringomyelia.

The following night, the patient developed increasing respiratory distress, requiring mechanical ventilation. Over the subsequent postoperative period, she failed multiple attempts at extubation. Extensive evaluation including infectious workup, chest x-ray, ultrasonography of the diaphragm, and upper airway endoscopy revealed no reason for her ongoing breathing difficulties. In addition, it was noted that the patient had not been able to move her upper extremities at any point during the day of surgery, or in the following days.

The neurology service was consulted again for further evaluation. Seven days after the initial surgery, the patient’s neurologic examination revealed flaccid paralysis of all 4 extremities, bifacial weakness, minimal gag reflex, and complete areflexia. She had full extracranial movements and normal pupillary response to light. Bulbar function was difficult to evaluate due to intubation. Repeat MRI of the brain and cervical spine revealed continued resolution of syringomyelia and no new abnormalities. A lumbar puncture showed mild albuminocytologic dissociation with protein of 90, 2 leukocytes, and 1 erythrocyte. IV immunoglobulin (IVig) therapy was instituted for presumed acute inflammatory demyelinating polyneuropathy.

On postoperative day 8, EMG and nerve conduction studies were completed. Nerve conduction studies revealed low compound motor action potentials in multiple nerves with preserved sensory nerve action potentials. There was no prolonged conduction velocity seen and normal F-wave responses were noted. EMG/needle study revealed increased insertional activity and positive sharp waves. The summation of these results suggested a possible diffuse motor axonal neuropathy or a presynaptic neuromuscular junction disturbance. Moreover, it did not fulfill criteria for a primary demyelinating neuropathy.

Based on EMG results, we performed a thorough evaluation of the patient’s skin and scalp. Along the superior retroauricular scalp, a 3-cm engorged tick was found and removed. This tick was identified by an infectious disease specialist as a gravid female Dermacentor species tick.

DISCUSSION Tick paralysis (TP) is a rare and easily reversible condition that if missed can lead to significant morbidity and mortality. In one series of children with TP between 1946 and 1906, 6% died. However, in the modern era of respiratory support and intensive care, survival may be higher. TP in the United States is more common in girls younger than 8 years with long hair, presumably due to the ability of the tick to go unnoticed on the scalp.

Most cases reported in the literature have been identified in Australia, where the causative species is *Ixodes holocyclus*. In North America, most cases reported in the Rocky Mountain region, US Pacific Northwest, and Southwestern Canada are transmitted by *Dermacentor andersoni* species and in the Southeast region are transmitted by *Dermacentor variabilis*.
These distinctions are relevant due to the differences in clinical presentation produced by the 2 species. Pupillary changes and focal weakness are more common in Australian cases (i.e., *Ixodes* cases). In addition, symptoms tend to remit immediately upon removal of a *Dermacentor* tick, whereas they persist for a day or two after removal of an *Ixodes* tick. Duration of recovery is more prolonged in Australian cases, often lasting days to weeks.1

TP is thought to be caused by a neurotoxin produced in the insect’s salivary glands. The toxin is thought to decrease presynaptic acetylcholine release at the neuromuscular junction, similar to botulinum toxin. It is possible that variations in the toxin of *Dermacentor* ticks compared to *Ixodes* ticks may account for the variation in clinical features.1

The classic clinical presentation of TP is an acute symmetric, ascending flaccid paralysis occurring over hours to days. There can be a prodrome of restlessness, irritability, fatigue, and myalgias, but fever is noticeably absent. Weakness usually begins in the lower extremity, and as the tick continues to feed, the weakness ascends from the legs to the arms and then to the muscles supplied by the cranial nerves, causing dysphagia, dysphonia, and facial weakness. Deep tendon reflexes are diminished or absent.1,5 A case series reported from Australia noted frequent pupillary involvement and external ophthalmoplegia in 2 of their patients, although this has not been the case in the United States.6 Respiratory involvement and requirement for mechanical ventilation occur invariably if the tick remains in place, though in some patients the tick may have fallen off, accounting for those patients who recover without assisted ventilation.1 Atypical presentations have been reported, including lower motor neuron facial nerve palsy, in which ticks were identified in the external auditory canal,7 and left-sided arm weakness in a brachial plexus distribution, which resolved after an engorged tick was removed from the subclavian fossa.8

TP presents as an acute-onset flaccid paralysis of the lower extremities with hyporeflexia or areflexia. Therefore, the differential diagnosis typically includes pathologies of the lower motor neuron or neuromuscular junction. See the table for full differential diagnosis.

The diagnosis of TP is made by finding the engorged tick on a patient with symptoms that correlate clinically. The importance of a complete skin evaluation including the scalp, external ear canals, groin, and axillae is irrefutable. Neuroimaging studies including CT and MRI are normal, although on closer inspection they may show the embedded tick if located on the scalp. CSF should also be normal.9 The albuminocytologic dissociation in our patient was believed to be postsurgical. If performed, electrophysiologic tests show a diffuse reduction in the compound muscle action potentials (CMAPs) with preserved sensory nerve action potentials. The low CMAPs are not usually accompanied by any abnormality of neuromuscular transmission with repetitive nerve stimulation testing. Published cases have proved that the function is reversible after removal of the tick.10

Despite attention to other tickborne diseases such as Lyme disease and Rocky Mountain spotted fever, TP remains a frequently misdiagnosed entity. A recent meta-analysis reviewed 50 cases of TP in the United States between 1946 and 2006 and revealed that 11 (22%) of these cases were initially misdiagnosed, with mean time to correct diagnosis of 2.16 days. Of these 11 cases, 9 were initially diagnosed as Guillain–Barré syndrome (GBS), 1 as chronic polynuropathy, and 1 as postinfectious polynuropathy. In this analysis, preparations for invasive IV therapy for GBS were initiated in 4 patients before tick attachment was discovered and 3 patients received IVlg, while 1 case was discovered during the process of placing a central catheter to prepare for plasmapheresis.4

The definitive treatment of TP is removal of the offending tick, after which symptoms rapidly resolve. Careful inspection of the rest of the body for additional ticks is mandatory. The tick should be carefully removed by grasping it as closely as possible to the attachment site and using steady traction to avoid leaving the head or mouthparts engaged.5 During paralysis, standard supportive therapy should be utilized, including mechanical ventilation when necessary for respiratory support.9 Antitoxin, a hyperimmune dog serum used in veterinary medicine, has been used in severe cases but carries a high risk of adverse reaction.6

**CASE SUMMARY** Within 24 hours after removal of the tick, our patient started to regain some movement in her upper and lower extremities. Within 48 hours, reflexes were elicited in the patella, ankles, biceps, and brachioradialis bilaterally. By 3 days after removal, she was extubated. She had normal facial strength but continued to have some weakness, primarily in the upper extremities, likely due in part to deconditioning. The patient was able to sit independently, feed

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**Table**: Differential diagnosis of tick paralysis1,5,6

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<thead>
<tr>
<th>Differential diagnosis of tick paralysis</th>
<th>Spinal cord compression</th>
<th>Transverse myelitis</th>
<th>Poliomyelitis</th>
<th>Myasthenia gravis</th>
<th>Organophosphate ingestion</th>
<th>Lambert-Eaton syndrome</th>
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herself, and walk with minimal assistance 6 days after tick removal and was discharged home.

AUTHOR CONTRIBUTIONS
Sarah L. Chagnon: corresponding author responsible for case report, literature review, and primary content of the manuscript. Monica Naik: coauthor responsible for revision of the manuscript. Hoda Abdel-Hamid: coauthor responsible for revision of the manuscript and execution and interpretation of EMG and nerve conduction studies.

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REFERENCES
Child Neurology: Brachial plexus birth injury
What every neurologist needs to know

ABSTRACT
While most often transient, brachial plexus birth injury can cause permanent neurologic injury. The major risk factors for brachial plexus birth injury are fetal macrosomia and shoulder dystocia. The degree of injury to the brachial plexus should be determined in the neonatal nursery, as those infants with the most severe injury—root avulsion—should be referred early for surgical evaluation so that microsurgical repair of the plexus can occur by 3 months of life. Microsurgical repair options include nerve grafts and nerve transfers. All children with brachial plexus birth injury require ongoing physical and occupational therapy and close follow-up to monitor progress. *Neurology* 2011;77:695-697

CASE PART 1 A term male infant was delivered to a gravida 3 parity 3 mother after an uncomplicated pregnancy. Labor was uneventful; however, delivery was complicated by shoulder dystocia. An episiotomy was performed and the infant’s posterior shoulder (left) was grasped and delivered, followed by the anterior shoulder (right). The infant weighed 4,750 g, >97th percentile for age. In the delivery room he was noted to have a left upper extremity palsy, with an asymmetric Moro reflex.

Differential diagnosis. Brachial plexus injury is the most common etiology of a plegic arm in the neonatal period. Other considerations include a clavicular or humeral fracture, with pain limiting limb movement. Fractures can be diagnosed by feeling for “step-offs,” crepitus, or pain along the bone and obtaining plain films. Central causes, such as a focal cortical dysplasia selectively affecting the arm area of motor cortex, are rare. Poland syndrome, the absence or hypoplasia of the pectoralis muscles, can cause monomorphic arm weakness; however, the structural abnormality is visibly apparent. A perinatal stroke typically does not cause hemiparesis in the neonatal period, but rather later in infancy.

CASE PART 2 On examination, there were no clavicular or humeral step-offs or crepitus, and a chest x-ray was normal. The parents were counseled that the brachial plexus injury would fully resolve. In pediatric follow-up at 2 months, however, the infant held the arm adducted and internally rotated at the shoulder. His forearm was pronated, his elbow extended, and his wrist and fingers were flexed in the “waiter’s tip” posture, consistent with injury affecting the C5-C7 root levels. There was no Horner syndrome. He was referred for neurologic and surgical evaluation.

Epidemiology. Brachial plexus birth injury occurs in 0.4 to 4 per 1,000 live births.1 It is most commonly associated with shoulder dystocia, an impaction of the infant’s anterior shoulder behind the maternal symphysis pubis. Lateral traction on the head, as part of the corrective maneuvers to deliver the infant, stretches the brachial plexus, leading to injury 4%–40% of the time.2

The strongest fetal risk factor for shoulder dystocia is macrosomia—birth weight greater than 4,000 g.2 Maternal risk factors for brachial plexus birth injury include diabetes or gestational diabetes, obesity, or a history of shoulder dystocia during a previous birth. A prolonged second stage of labor (pushing) and operative vaginal delivery also increase the risk.1,3 However, half of the cases have no identifiable risk factor.4

While the risk factors for shoulder dystocia are well recognized, they have poor predictive value.3,4 C-section decreases, but does not eliminate, the risk of brachial plexus injury, and introduces additional maternal morbidity.1,2

See page 698

From the School of Medicine (C.B.P.), Department of Obstetrics and Gynecology (A.C.J.), Department of Genetics (A.C.J.), Department of Neurology, Division of Child Neurology (A.A.G.), University of California, San Francisco; and Department of Surgery (J.R.C.), Massachusetts General Hospital, Boston.

Disclosure: Author disclosures are provided at the end of the article.
Neuroanatomy and prognosis. The ventral rami of the C5 through T1 spinal nerves form the roots of the brachial plexus. Children with brachial plexus birth palsy have traditionally been classified clinically into 4 groups. The largest group (50% of cases) involves C5-C6 injury, classic Erb palsy, and generally has the best prognosis. The next group (25%) involves C5-C7 injury and has an intermediate prognosis. Children in these 2 groups hold the arm in adduction and internal rotation at the shoulder due to relative sparing of the shoulder adductor and internal rotation muscles. The imbalance of push-pull muscular forces across the glenohumeral joint at the shoulder causes the joint itself to develop abnormally, with increasing deformity as the child grows.1 Involvement of C7 is suggested by the presence of a wrist drop.

The third and fourth groups (together 25%) involve injury to the entire plexus. The arm is held in a neutral position with little to no movement. The fourth group is the most severely affected and can be distinguished by the presence of an ipsilateral Horner syndrome (miosis, ptosis, and anhidrosis) due to concurrent injury to the sympathetic chain as it exits the spinal cord.1 Isolated lower root injury (C8-T1), Klumpke palsy, is extremely rare.6

Brachial plexus injuries can also be classified by the type of neuropathologic injury. The least severe is neurapraxia, or stretch injury, causing conduction block, but no permanent structural damage to the nerve. Conduction block can last for hours to weeks, but ultimately fully recovers. Axonotmesis injury involves damage to axons, as well as supporting blood vessels and connective tissue, including perineurium and epineurium. If only the axons are disrupted, they regrow with full recovery. If the perineurium or epineurium are also disrupted, the likelihood of complete recovery decreases significantly. Neurotmesis injury indicates complete nerve rupture. Scar tissue forms between the proximal and distal ends of the nerve to become a neuroma. Recovery is limited because it is difficult for axons to regenerate through the neuroma. Root avulsion is the most severe injury, usually occurring at the nerve rootslet at or near the spinal cord.7 Avulsion injuries do not spontaneously recover so it is essential that these patients be identified for early intervention.4,8

When examining the brachial plexus in a neonate, the emphasis should be on looking for signs of injury to proximal nerve structures as these are highly suggestive of avulsion. Given the proximity of the sympathetic chain to the spinal cord, the presence of Horner’s almost always implies a root avulsion injury. Additional signs of avulsion include winging of the scapula, indicating long thoracic nerve injury, and asymmetry in chest wall excursion, indicating phrenic nerve injury. In cases of complete plexus palsy, a chest x-ray should be performed to rule out hemidiaphragm paralysis.

Diagnostics. The diagnosis of brachial plexus birth injury and the assessment of severity are both made clinically based on history and examination findings.

Some groups support the routine use of EMG/NCS or MRI for diagnosis early in the patient’s course to confirm the presence of avulsion-type injuries4; however, as the decision to intervene surgically is exclusively based on whether there is adequate recovery on physical examination over time, these studies typically do not aid clinical decision-making.

Therapeutics. In the first few days of life, the patient’s arm can be temporarily immobilized via swaddling if there is pain from an accompanying fracture. Caregivers should be instructed in appropriate positioning to avoid contractures, pressure ulcers, and unnecessary traction.10 If the patient tolerates it, gentle range of motion exercises may be started either immediately or at least by 7 to 10 days of life. Physical therapy should be continued until the child’s brachial plexus injury recovers.1,6 For cases that result in permanent functional deficit, therapy should be tailored to the patient’s age and developmental stage.10

Ideally, infants with brachial plexus injuries should be referred to a multidisciplinary specialty clinic for treatment. Teams at these clinics include pediatric neurologists, orthopedic surgeons, neurosurgeons, physical and occupational therapists, and social workers. If this is not possible, the infant should be followed closely by a neurologist to monitor the pace and extent of neurologic recovery. If antigravity biceps function does not return before 6 weeks of age, a referral to surgery is appropriate, as a subset of these infants will require microsurgical reconstruction of the plexus. In cases of suspected avulsion or rupture injuries where spontaneous recovery is impossible or unlikely, it is generally agreed the infant should undergo microsurgical reconstruction by age 3 months for avulsions and by 6 months for nerve ruptures.1 Early surgery minimizes motor endplate loss and maximizes recovery time.

In less severe injuries, the indications for, and timing of, surgical interventions remain controversial. Most groups agree that lack of antigravity biceps function by 3 to 6 months is an indication for surgical intervention, while others continue to observe and operate as late as 9 or 10 months of age.1

Surgical intervention for brachial plexus palsy includes early microsurgical repair of the brachial plexus using nerve grafts or nerve transfers. In both
cases, the neuronal scar tissue (neuroma) is resected. For rupture injuries, a donor nerve, most often the sural nerve, is inserted into the area of discontinuity. Nerve transfers, in contrast, redirect an uninjured healthy nerve, such as the spinal accessory nerve (CN XI), to the distal site of nerve injury and rely on neuroplasticity for adoption of functional control by the transferred nerve.  

Outcomes. Most children with brachial plexus birth palsy recover well. A recent prospective study demonstrated full recovery in 50% of patients by 3 months of age, and 82% by 18 months. However, roughly one in 5 affected infants have some degree of permanent nerve damage.  

While patients with permanent injury have lower functional scores than their peers, these children have equivalent rates of individual and team sports participation as their peers. Most children with persistent injury can manage their activities of daily living, albeit with varying degrees of difficulty.  

CASE PART 3 The infant regained gravity-assisted biceps function at 3 months of age and antigravity biceps function at 5 months. Now 18 months old, he is able to use his left hand and arm, though still with weakness and range of motion limitations. He continues with intensive physical and occupational therapy and his ultimate outcome is not yet determined.

DISCUSSION Brachial plexus birth injuries are usually transient, but can result in permanent functional deficits. Signs of nerve root avulsion, indicating severe injury that will not recover spontaneously, include a total plexopathy (complete arm paralysis), Horner syndrome, or phrenic nerve involvement. These injuries should be referred for microsurgical evaluation immediately so that reconstruction of the plexus, if indicated, can be performed by 3 to 6 months. All infants with brachial plexus nerve injuries need close follow-up to monitor progress, and early and ongoing physical and occupational therapy to maintain range of motion, prevent glenohumeral joint deformity, and maximize function.

AUTHOR CONTRIBUTIONS
Dr. Pham: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Kratz: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, acquisition of data. Dr. Jelin: drafting/revising the manuscript. Dr. Gelfand: drafting/revising the manuscript.

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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: An unusual cause of transverse myelitis?

SECTION 1

A 71-year-old woman presented with a 1-week history of progressive weakness involving her lower extremities, leading to an inability to walk. She also noticed diminished sensation in her lower extremities. She did not complain of bowel or bladder dysfunction. She did not have any neurologic symptoms in her upper extremities. She experienced an upper respiratory tract infection 5 days prior to the start of these symptoms and was treated with antibiotics. There was no history of headache, impaired cognition, or speech impairment.

Her examination revealed normal higher mental functions and intact cranial nerve function bilaterally. She had increased tone in both lower extremities, and muscle strength was 3/5 at the hips and 2/5 at the knees and ankles. The weakness was in a pyramidal distribution with the flexors more affected than extensors. Sensory examination revealed diminished vibration and joint position sense up to her knees; a sensory level for fine touch and pinprick was detected at approximately the T6 level. She had exaggerated reflexes in her lower extremities with no clonus and had extensor plantar responses bilaterally.

Questions to consider:
1. What is the localization of the problem?
2. What are the likely etiologies?
3. What would you do next?

The involvement of multiple long tracts, increased tone, hyperreflexia, sensory level at T6, and no symptoms or signs in the upper extremities point to a lesion in the thoracic spinal cord.

The evolution of these complaints over a week would make a vascular etiology unlikely, and the differential for this patient includes demyelinating, inflammatory, infectious, neoplastic, compressive, and metabolic causes. In a patient presenting with an acute onset of clinical features consistent with a myelopathy, an urgent MRI of the spine with contrast should be obtained to rule out intervention.

An MRI of the spine was obtained, which demonstrated a longitudinally extensive intramedullary spin cord lesion extending from T6 to T12 (figure). Due to her compromised renal function, gadolinium contrast could not be administered. A diagnosis of transverse myelitis, possibly postinfectious, was made, and she was started on IV methylprednisolone 1 g daily for 5 days.

Questions to consider:
1. Given the MRI findings, what would the differential diagnosis be?
SECTION 4
Repeat imaging showed some progression of the longitudinal extent of the spinal cord lesion and splayed brain lesions. At this point, a brain biopsy was considered, given the lack of response to therapy directed at inflammatory and demyelinating disease.

Brain biopsy of a frontal lobe lesion was performed and revealed metastatic small-cell carcinoma. CT chest was then done and revealed a left hilar mass suggestive of a neoplasm. The hilar mass was not biopsied due to the positive brain biopsy and radiologic appearance of the mass. A diagnosis of longitudinally extensive spinal cord lesion secondary to intramedullary metastasis from stage IV small-cell lung cancer was made. She was seen by the oncology service and chemotherapy was initiated. However, she continued to worsen and was ultimately transferred to hospice.

DISCUSSION
LETM has a broad differential diagnosis. However, the most common causes of LETM are inflammatory demyelinating diseases such as NMO and postinfectious encephalomyelitis. The presence of numerous brain lesions makes NMO less likely, though brain lesions may occur in patients with NMO, producing the so-called NMO spectrum disorder (NMOSD).6 NMOSD brain lesions are usually asymptomatic and may consist of periependymal lesions around the ventricular system, extensive hemorrhagic lesions, and lesions in the internal capsule and cerebral peduncles.7 NMO immunoglobulin G or aquaporin-4 antibody positivity was included in the diagnostic criteria for NMO in 2006 and improved recognition of the disease. It should be noted that the sensitivity of NMO IgG varies in different series from 51% to 90%, while its specificity lies between 91% and 100%.

Postinfectious encephalomyelitis can cause LETM and brain lesions, similar to those of our patient. A recent prospective study described the clinical features and course of postinfectious neurologic syndromes.8 These ranged from isolated encephalitis or myelitis to more diffuse encephalomyeloradiculoneuritis. Patients with postinfectious neurologic syndromes were older, had more severe neurologic disability at onset and poorer outcomes, and were more resistant to steroid treatment than patients with MS.9 In contrast to our patient, almost 90% of patients with postinfectious neurologic syndromes had elevated CSF counts suggesting inflammation, in addition to elevated CSF protein levels.

Intramedullary spinal cord metastases presenting as LETM are rarely encountered.10 Intramedullary spinal cord metastases are seen in only 0.1%–0.4% of cancer patients.10 In a recent retrospective review of intramedullary spinal cord metastases, they were the presenting feature in 20% of patients.11 The underlying malignancy was lung cancer in 50%, followed by renal carcinoma, breast cancer, and melanoma. Almost all intramedullary spinal cord metastases in this review exhibited enhancement with gadolinium and had extensive edema on T2-weighted sequences above and below the metastasis.11 In our patient, the diagnosis might have been facilitated if gadolinium contrast had been administered, as this could have revealed an enhancing nodule within the longitudinally extensive spinal cord lesion.

Some of the clues pointing us away from an inflammatory cause in our patient were the patient’s advanced age, lack of pleocytosis in the CSF, and lack of response to steroids and plasma exchange. It should also be noted that in our case the term “myelitis” is a misnomer, since there is no inflammatory lesion of the cord. This case highlights the importance of recognizing the broad differential diagnosis of LETM and appropriately utilizing invasive tests such as brain biopsy when patients do not have the expected response to therapy, especially when imaging and laboratory studies do not fully support the working diagnosis.

AUTHOR CONTRIBUTIONS
Dr. Bhargava conceptualized and drafted the manuscript. Dr. Elble critically revised the manuscript for important intellectual content.

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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 Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.

Clinical Reasoning:
A 55-year-old woman with vertigo
A dizzying conundrum

SECTION 1
A 55-year-old woman presented to the emergency department complaining of dizziness. Several hours earlier she abruptly felt "the room spinning and moving back and forth." Simultaneously, she experienced nausea, vomiting, and gait unsteadiness. The dizziness exacerbated with head movement. She denied head or neck pain, photophobia, phonophobia, auditory symptoms, weakness, numbness, diplopia, dysarthria, dysphonia, dysphagia, history of recent illness, prior dizziness, or headache. Medical history included hyperlipidemia and hypertension.

Question for consideration:
1. What is the differential diagnosis for acute vertigo?

To determine the cause of acute vertigo, it is important to know whether it is transient (seconds to minutes) or prolonged (hours to days); a single episode of vertigo or a recurrence; if it is positionally provoked (e.g., benign paroxysmal positional vertigo); and if there are any accompanying symptoms or signs. The most common causes of acute prolonged vertigo include a peripheral vestibulopathy. Ménière syndrome, migrainous vertigo, or brainstem or cerebellar ischemia. This discussion is limited to the distinction between a peripheral vestibulopathy and ischemia.

The acute vestibular syndrome (AVS) develops over seconds to hours and is characterized by vertigo, nausea, vomiting, gait instability, head motion intolerance, and nystagmus. It is caused by either an acute peripheral vestibulopathy (APV) or brainstem/cerebellar ischemia, and similarities in presentation often make the distinction a diagnostic challenge. Transient ischemic attacks can cause acute vertigo with rapid resolution but vertigo resulting from a

GO TO SECTION 3
SECTION 3
In an acute destructive lesion affecting 1 labyrinth, such as an APV, symptoms result from ipsilateral afferent hypovascularity and relative contralateral hyperactivity from the vestibulocochlear nerve. During a normal head turn to the left, there is left-greater-than-right asymmetry in afferent vestibular signals and the eyes drift to the right to maintain stable vision (i.e., vestibulo-ocular reflex or VOR). A right APV is perceived as a leftward head turn even though the head is still. As a result, the eyes continuously drift to the right (slow phase of nystagmus), and a position reset mechanism (fast phase) quickly brings the eyes back to the left (to midline) (figure 1). The nystagmus is of larger amplitude when gazing in the direction of the fast phase (i.e., Alexander law). The horizontal component of peripheral vestibular nystagmus is inhibited with fixation (there is a poor torsional fixation mechanism), which does not occur with central causes of vestibular nystagmus.

Since the intensity of peripheral nystagmus is influenced by fixation, observation under various conditions can help distinguish central vs peripheral causes of vertigo as peripheral nystagmus inhibits with fixation, and conversely, increases with fixation removed. Oculomotor funduscopic examination is performed by visualizing the optic disc with an ophthalmoscope and then covering the patient's viewing eye, thus removing fixation, which enhances peripheral nystagmus but has no effect on central nystagmus.

Similarly, the penlight cover test involves having the patient fixate on a penlight, and then covering 1 eye, thus removing fixation as the uncovered eye continues to view only the bright penlight. Having the patient view a featureless scene such as a piece of white paper has a similar effect: since there is no feature available for foveation, fixation is suppressed.

Dynamic assessment of the vestibular system includes the HIT, which tests angular VOR function (figure 2). Although a peripheral pattern of nystagmus with an abnormal HIT implies labyrinthine or vestibular nerve dysfunction, it is important to recognize that the etiology may be ischemia. The vascular supply to the inner ear is via the internal auditory artery, so a "peripheral" lesion can be from infarction.

Another important sign to look for in the AVS is a skew deviation, which is a nonparalytic nystagmus vertical ocular misalignment due to an imbalance of utricular inputs to the oculomotor system. It is often accompanied by features of the ocular tilt reaction (OTR), which includes the triad of skew deviation, head tilt, and ocular counterroll. A skew deviation is best demonstrated during alternate cover testing demonstrating vertical correction of the uncovered eye to maintain fixation, or subjectively with Maddox rod testing. A skew deviation and a fourth nerve palsy may present similarly (figure 3). A skew deviation occurs most

Figure 1  Pathophysiology of peripheral nystagmus in an acute peripheral vestibulopathy

Nystagmus from an acute peripheral vestibulopathy (APV) is mixed horizontal-torsional, indicating a lesion of the entire vestibular nerve or all semicircular canals within one labyrinth. Stimulation of individual canals move the eyes in distinct planes (i.e., horizontal, vertical, or torsional). In a right APV, the direction of nystagmus is determined by the intact left labyrinth: the 2 oppositely oriented left anterior and posterior canals cancel out vertical movement, leaving only a slight torsional component contributed from each, while the horizontal vector is attributable to the unopposed left horizontal canal. This generates a slow (pathologic) phase (in red) toward the affected ear with a fast (position reset) phase (in black) away from the affected ear. Nystagmus is named for the direction of the fast phase. The nystagmus is present in primary position and beats in the same direction (unidirectional) with gaze to either side. LAC = left anterior semicircular canal; LHC = left horizontal semicircular canal; LPC = left posterior semicircular canal; RAC = right anterior semicircular canal; RHC = right horizontal semicircular canal; RPC = right posterior semicircular canal. Redrawn and modified from Leigh RJ, Zee DS. The Neurology of Eye Movements (Contemporary Neurology Series), 4th ed. New York: Oxford University Press, Inc.; 2006: figure 2-2. By permission of Oxford University Press, Inc.
(A) Normally, during a quick 20° head turn to the right, the patient will be able to maintain fixation on the examiner's nose (i.e., the target). (B) With a right peripheral vestibulopathy, when the head is turned quickly to the right, the line of sight moves with the head due to a hypoactive VOR, necessitating a compensatory catch-up saccade to the left to refixate on the examiner's nose. Reprinted from: Edlow JA, Newman-Toker DE, Savitz SI. Diagnosis and initial management of cerebellar infarction. Lancet Neurol 2008;7:951-964. With permission from Elsevier.

commonly with brainstem or cerebellar lesions, but also may be seen with a lesion anywhere from the utricle to the interstitial nucleus of Cajal in the rostral midbrain.11

Other signs of central localization of acute vertigo include direction-changing (i.e., gaze-evoked or bidirectional) nystagmus, pure horizontal, torsional, or vertical nystagmus, impaired or asymmetric smooth pursuit, inability to suppress the VOR (combined eye-head tracking of moving targets), dysmetric saccades, and associated brainstem and long tract signs.17

In our patient, blood pressure was 143/79 mm Hg and general medical examination including otoscopy were normal. In primary gaze there was left-beating horizontal-torsional jerk nystagmus that intensified with left gaze, and lessened but remained left-beating in right gaze (video, first half, on the Neurology® Web site at www.neurology.org). The nystagmus intensified with removal of fixation during occlusive funduscoppy and the penlight cover test. The HIT was normal to the left but abnormal to the right (video, second half), demonstrating a catch-up saccade, confirming a hypoac-
(A) Left fourth nerve palsy compared with (B) skew deviation. By convention, the Maddox rod is placed over the right eye. In both (A) and (B) there is a vertical misalignment in primary gaze with the left eye higher than the right (i.e., left hypertropia). A left fourth nerve palsy is diagnosed in (A) by demonstrating greater vertical separation between the light and the horizontal line (i.e., greater degree of left hypertropia) in contralateral gaze (with the paretic eye adducted), downgaze, and ipsilateral head tilt (not shown). A left hypertropia caused by a skew deviation in (B) is typically comitant, meaning the degree of vertical misalignment is consistent in all directions of gaze. In contrast to the head tilt seen in a fourth nerve palsy, which is compensatory (i.e., a contralateral head tilt minimizes ocular misalignment due to impaired intorsion of the affected eye), the head tilt in the OTR occurs in the same direction as the cyclo torsion (ocular counterroll). Reprinted from: Kheradmand A, Bronstein A, Zee DS. Clinical bedside examination. In: Eggers SD, Zee DS, eds. Vertigo and Imbalance: Clinical Neurophysiology of the Vestibular System: Handbook of Clinical Neurophysiology. New York: Oxford University Press, Inc; 2012: figure 2 (in press 2012). By permission of Oxford University Press, Inc.

Questions for consideration:
1. What are the most common manifestations of cerebellar ischemia?
2. What are the 3 most important bedside ocular motor tests to differentiate a stroke from an APV?
3. How has the examination narrowed the differential diagnosis in this patient?

GO TO SECTION 4
### Table

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Peripheral</th>
<th>Central</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystagmus</td>
<td>Unidirectional; mixed horizontal-torsional; obeys Alexander’s law; slow phase with constant velocity; more intense when lying with affected ear down</td>
<td>May change direction; pure horizontal, torsional, or vertical; slow phase with constant, increasing or decreasing velocity</td>
<td>Peripheral nystagmus suppresses with fixation and increases with fixation removal, while central nystagmus is poorly suppressed by fixation.</td>
</tr>
<tr>
<td>Head impulse test</td>
<td>Abnormal</td>
<td>Typically normal</td>
<td>Lesions of the vestibular nucleus, root entry zone of 8th cranial nerve, or caudal cerebellum may cause an abnormal head impulse test.</td>
</tr>
<tr>
<td>(horizontal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skew deviation</td>
<td>Absent</td>
<td>May be present</td>
<td>Rarely, a small skew may be apparent from a utricular lesion, but a large skew with diplopia suggests central localization.</td>
</tr>
<tr>
<td>Associates symptoms or</td>
<td>Hearing loss or tinnitus, minor gait instability, and veering toward the side of the lesion</td>
<td>Headache or neck pain, particularly concerning if abrupt onset, prolonged, or severe; weakness, nuchal pain, diplopia, dysarthria, dysphagia, Horner sign, drop attack (abrupt fall with preserved level of consciousness), incoordination, marked gait instability, and lateropulsion</td>
<td>A central lesion presents uncommonly as isolated vertigo.</td>
</tr>
<tr>
<td>signs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SECTION 4

In a series of 66 patients with isolated cerebellar infarctions, vertigo and lateropulsion (defined as an irresistible sensation of falling to one side) were the most common symptoms. Although vertigo and lateropulsion can each occur in isolation with a cerebellar stroke, other signs and symptoms are typically present, including limb ataxia, nausea/vomiting, truncal ataxia, dysarthria, nystagmus, headache, confusion, or somnolence.

A stroke in the posterior inferior cerebellar artery territory can cause a “pseudovestibular neuritis” manifesting as isolated vertigo without auditory or other symptoms, but typically has a normal HIT. A superior cerebellar artery stroke can cause a “pseudoincipient” picture because of gait or truncal ataxia with dysarthria, or “pseudogastroenteritis” with nausea and vomiting.

The internal auditory artery (IAA) is an end artery from the anterior inferior cerebellar artery (AICA) that supplies the vestibulocochlear nerve, cochlea, and vestibular labyrinth. Due to a paucity of collaterals, the IAA is vulnerable to ischemia. A labyrinthine infarction usually presents with sudden loss of hearing and vertigo accompanied by other AICA-territory signs (e.g., cerebellar, lateral pontine, or midbasilar syndromes). However, isolated labyrinthine ischemia may herald AICA infarction. In a series of 82 patients with AICA strokes, 80 had acute prolonged vertigo and vestibular dysfunction of peripheral, central, or combined origin; 35 had acute prolonged vertigo with audiovestibular loss; 24 had acute prolonged vertigo without audiovestibular loss, while a selective loss of vestibular (4) or cochlear (3) function was much less common. AICA strokes have also been referred to as “pseudolabyrinthitis.”

In patients presenting with the acute vestibular syndrome, the combination of direction-changing nystagmus, skew deviation, and normal HIT were more sensitive in detecting stroke than MRI (table). A normal HIT strongly indicates a central process, but an abnormal HIT is a less reliable indicator of a peripheral lesion because of APV mimics (i.e., ischemia of the vestibular nucleus, root entry zone of the eighth cranial nerve, or caudal cerebellum may cause an abnormal HIT). In addition to the findings on bedside examination, vertigo due to cerebrovascular disease should be considered if any of the following factors are present: stroke risk factors, risk of vertebral artery dissection, abrupt onset, inability to ambulate, paucity of nausea and vomiting with marked gait instability or severe nausea and vomiting with little gait instability, or other accompanying central neurologic symptoms and signs.

Our patient had a right APV without auditory symptoms, and was diagnosed with vestibular neuritis. Prior to evaluation by the authors and within 24 hours of symptom onset, a brain MRI was found to be normal. Although brainstem/cerebellar infarctions may be missed acutely on MRI, the positive HIT, unidirectional nystagmus, and absent skew deviation all pointed away from a central process, and therefore an MRI was arguably unnecessary. Her symptoms improved significantly over several days with only antiemetics, and vestibular rehabilitation was recommended.
AUTHOR CONTRIBUTIONS
Daniel R. Gold, DO: conceptualization, drafting, and revising the manuscript. Stephen G. Reich, MD: drafting and revising the manuscript.

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REFERENCES
Education Research

As the central mission of *Neurology*, education is a top priority. This is a section for interventional educational studies, as well as more traditional educational research, such as surveys. This section will examine the way neurologists not only practice, but also the way we teach and approach education. Neurologists have traditionally been respected, perhaps above all other specialties, for their scholarship and teaching. Educational issues will therefore continue to be at the center of the mission of *Neurology*. 
Education Research:
Case logs in the assessment of medical students in the neurology outpatient clinic

ABSTRACT

Objective: Using outpatient neurology clinic case logs completed by medical students on neurology clerkships, we examined the impact of outpatient clinical encounter volume per patient on outcomes of knowledge assessed by the National Board of Medical Examiners (NBME) Clinical Neurology Subject Examination and clinical skills assessed by the Objective Structured Clinical Examination (OSCE).

Methods: Data from 394 medical students from July 2008 to June 2012, representing 9,791 patient encounters, were analyzed retrospectively. Pearson correlations were calculated examining the relationship between numbers of cases logged per student and performance on the NBME examination. Similarly, correlations between cases logged and performance on the OSCE, as well as on components of the OSCE (history, physical examination, clinical formulation), were evaluated.

Results: There was a correlation between the total number of cases logged per student and NBME examination scores ($r = 0.142; p = 0.005$) and OSCE scores ($r = 0.136; p = 0.007$). Total number of cases correlated with the clinical formulation component of the OSCE ($r = 0.172; p = 0.001$) but not the performance on history or physical examination components.

Conclusion: The volume of cases logged by individual students in the outpatient clinic correlates with performance on measures of knowledge and clinical skill. In measurement of clinical skill, seeing a greater volume of patients in the outpatient clinic is related to improved clinical formulation on the OSCE. These findings may affect methods employed in assessment of medical students, residents, and fellows. *Neurology* 2014:82:e138–e141

GLOSSARY

NBME = National Board of Medical Examiners; NSUHS = NorthShore University Health System; OSCE = Objective Structured Clinical Examination; SP = standardized patients; UCMC = University of Chicago Medical Center.

There has been an emphasis at medical schools and residency programs on providing increased outpatient exposure.¹ It remains to be seen how to best evaluate these experiences during training to ensure their adequacy. An easily applicable method of measuring clinical experience is via case logs of patient encounters. Case logs provide objective data at low cost, provide a measure of volume and breadth of experience, and can be scored quickly. Pitfalls include that they rely on self-reporting, are potentially time-consuming for the individual completing them, and may provide no specific information on the trainees’ medical knowledge or clinical acumen. Establishing validity for the use of case logs has consequences for medical student training.

One previous study evaluating case logs as assessment tools in neurology clerkships has been published, showing no correlation between the total number of inpatient and outpatient cases recorded per student and performance on an internally developed written examination.² Additional studies evaluating student performance in other specialties have found no correlation between number of patient encounters documented in case logs and either National Board of Medical Examiners (NBME) clinical subject examination scores or internally developed examinations.³,⁴ While case logs have long played an important role in the assessment of surgical trainees, there is a paucity of data on their use in the evaluation of trainees from non–procedurally oriented specialties.

METHODS

This project was submitted to the University of Chicago Institutional Review Board and was deemed exempt from review.

Students at the University of Chicago Pritzker School of Medicine completing a required 4-week neurology clerkship are assigned to University of Chicago Medical Center (UCMC) or NorthShore University Health System (NSUHS), a community-based teaching hospital.

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¹From the Department of Pediatrics, Section of Pediatric Neurology (D.V.A.), and Department of Neurology (J.R.B., C.A., R.V.L.), University of Chicago, IL.

²Go 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.
affiliate. During the approximately week-long outpatient clinical portion of the clerkship, students are required to keep case logs of outpatient encounters. Students obtain a sticker from the patient’s clinic encounter sheets and place it in a logbook maintained by the student. Six students (1.5%) did not log any cases. These students were not included in analyses. Students are requested to document diagnosis or chief complaint of each patient encounter, and 98% (n = 9,600) of logged patient encounters included this. Additional components of our preexisting assessment methods include the NBME Clinical Subject Examination, a nationally available standardized examination of knowledge in neurology, and the Neurology Objective Structured Clinical Examination (OSCE), an internally developed examination of clinical skill in neurology that we have previously described. 14 The OSCE score is derived from 3 components. The first 2 are scored by standardized patients (SP) via completion of a checklist evaluating performance of key elements of history taking and physical examination. The third component is a clinical formulation scored by faculty raters using a checklist reviewing an online write-up completed by students after evaluating the SP. The write-up includes the history, physical examination, assessment, and management plan.

Case logs, NBME clinical subject examination scores, and OSCE scores for all 394 students (362 third year, 32 fourth year) who logged cases from July 2008 to June 2012 were analyzed. Prior to analysis, data were anonymized. Pearson correlations were performed to evaluate the total number of patient encounters recorded by a given student and his or her score on the NBME subject examination. A similar analysis was performed to test for correlation of patient encounters with overall OSCE scores. Additional analyses evaluating the number of patient encounters per student and performance on the 3 distinct components of the OSCE score were performed.

Finally, an exploratory analysis was performed evaluating the breadth of clinical presentations encountered by students in the outpatient neurology clinic. Case logs were reviewed and all recorded chief complaints/diagnoses were tabulated and classified into the following categories: seizure, cerebrovascular disease, peripheral/neuromuscular, spinal disease/neck/back pain, CNS demyelinating disease/neuroimmunology, headaches, sleep disorders, neuro-oncology, movement disorders, dementia, other neurodegenerative disorders, and other. If more than one diagnosis or chief complaint was listed, the first one listed was used in the tabulation.

RESULTS Students logged a mean of 24.8 cases (range 6–34, SD 5.4). Hierarchical analysis found no difference (p = 0.3) between the number of cases recorded between third (mean = 24.9, SD = 5.4) and fourth year (mean = 24.7, SD = 6.1) students. Comparison between the 2 clinical sites, UCMC (306 students) and NSUHS (88 students), demonstrated a difference in the number of cases seen. Students assigned to NSUHS recorded a mean of 26.9 (SD 5.0) cases per student compared to 24.3 (SD 5.4) at UCMC (p = 0.02). The difference in total number of cases logged per student is likely due at least in part to the number of days spent in the outpatient clinic at the 2 respective sites. The mean number of days in the outpatient clinic for students assigned to UCMC was 4.8 in comparison to 6.3 for students assigned to NSUHS. This small statistically significant difference in length of the ambulatory rotation was not associated with a difference in NBME scores between students assigned to the 2 sites (p = 0.77). However, there was a modestly greater mean OSCE score in students assigned to the UCMC clinical site (r = 2.3; df = 392, p = 0.02). The students logged a range of case types (table 1). The most frequently logged categories were other (n = 1,608 cases), which consisted of a variety

<table>
<thead>
<tr>
<th>Category</th>
<th>Sum of cases logged</th>
<th>No. of students logging case type</th>
<th>Mean cases per student logging cases in this category</th>
<th>Standard deviation</th>
<th>Maximum no. of cases logged per student</th>
</tr>
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<tr>
<td>Total</td>
<td>9,761</td>
<td>394</td>
<td>24.85</td>
<td>5.416</td>
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<tr>
<td>Other</td>
<td>1,608</td>
<td>369</td>
<td>4.36</td>
<td>2.295</td>
<td>14</td>
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<tr>
<td>Neuro-oncology</td>
<td>1,608</td>
<td>344</td>
<td>4.67</td>
<td>2.356</td>
<td>13</td>
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<td>CNS demyelinating/neuroimmunology</td>
<td>1,190</td>
<td>322</td>
<td>3.70</td>
<td>2.521</td>
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<tr>
<td>Peripheral/neuromuscular</td>
<td>1,163</td>
<td>337</td>
<td>3.45</td>
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<td>Epilepsy</td>
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<td>315</td>
<td>3.34</td>
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<td>266</td>
<td>2.89</td>
<td>2.029</td>
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<td>Headaches</td>
<td>746</td>
<td>291</td>
<td>2.56</td>
<td>1.740</td>
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<td>Cerebrovascular</td>
<td>384</td>
<td>202</td>
<td>1.90</td>
<td>1.230</td>
<td>9</td>
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<tr>
<td>Sleep disorders</td>
<td>357</td>
<td>122</td>
<td>2.93</td>
<td>2.329</td>
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<td>Spine/neck/back pain</td>
<td>284</td>
<td>184</td>
<td>1.54</td>
<td>0.968</td>
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<tr>
<td>Other neurodegenerative disorders</td>
<td>276</td>
<td>160</td>
<td>1.73</td>
<td>1.288</td>
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<tr>
<td>Dementia</td>
<td>164</td>
<td>109</td>
<td>1.50</td>
<td>0.878</td>
<td>5</td>
</tr>
<tr>
<td>Not listed</td>
<td>191</td>
<td>77</td>
<td>2.48</td>
<td>3.255</td>
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### Table 2  
**Case Log/Objective Structured Clinical Examination correlations**

<table>
<thead>
<tr>
<th></th>
<th>History</th>
<th>Physical examination</th>
<th>Clinical formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pearson correlation</strong></td>
<td>0.029</td>
<td>0.063</td>
<td>0.172*</td>
</tr>
<tr>
<td><strong>Significance (2-tailed)</strong></td>
<td>0.560</td>
<td>0.211</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

Correlations between cases logged per student and scores on the history, physical examination, and clinical formulation components of the Objective Structured Clinical Examination.

* Correlation is significant at the 0.01 level (2-tailed).

of neurologic conditions including behavioral problems, infections, congenital abnormalities, and psychogenic symptoms, and neuro-oncology (n = 1,608 cases). The least frequently encountered categories were dementia (n = 164) and other neurodegenerative disorders (n = 276).

The mean NBME score for all students was 77.77 (range 55–99). A significant relationship was demonstrated between number of patients recorded via case logs and NBME subject examination scores ($r = 0.142, p = 0.05$). The mean NBME subject examination score in the cohort of students logging the lowest quartile of cases (6–21 cases) was 76.23, the second quartile (22–26 cases) was 77.61, the third quartile (27–29 cases) was 78.78, and the fourth quartile (30–34 cases) was 78.61. Thus, a difference of 2.38 points on the mean NBME subject examination score exists between the lowest case logging quartile and the highest. This 2.38-point difference in average absolute NBME score between students seeing fewer vs greater cases in the outpatient clinic corresponds to a difference of about 10 percentile points in the score distributions reported by the NBME, representing a modest but considerable improvement in student performance. A similar relationship was also found with regards to number of cases recorded and OSCE scores ($r = 0.136, p = 0.007$). When evaluating the relationship between patients recorded per student via case logs and scores on 3 distinct components of the OSCE, a correlation was found only on the faculty-graded clinical written formulation component ($r = 0.172, p = 0.001$) (table 2).

### DISCUSSION

We present evaluations of correlations in medical students between patient encounters documented via case logs and performance on national standardized examinations of knowledge and validated examinations of clinical skill in a specialty. Outpatient clinical experiences occurred either at an academic medical center or a community medical center, making findings relevant to a range of clinical education settings. While these findings specifically reflect our analyses of medical students in a neurology clerkship, it would be reasonable to hypothesize that similar relationships between volume of cases seen and performance on standardized examinations of knowledge and clinical skill would be present in other medical student clerkships and non-procedure-oriented residency/fellowship programs. Of particular interest is that the correlation between number of cases recorded per student and performance on the OSCE was due exclusively to performance on the written clinical formulation component of the evaluation, reflecting students' skills in reporting and analyzing clinical findings. There was no relationship between case volume and the components of the OSCE that evaluate thoroughness of history taking and physical examination. We hypothesize that by directly observing expert clinicians evaluating patients with a wide range of complaints and underlying pathologies, trainees gain valuable experience in formulating their own thoughts and developing management plans with respect to clinical encounters. By understanding the correlations between volume of patients encountered and students' outcomes on specific performance measures, we can work on tailoring the outpatient experience to best achieve our educational goals. As the outpatient experience represents only a single component of a

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Albert et al.1 examined the relationship between number of cases encountered by medical students in a 1-week outpatient component of a 4-week neurology clerkship and performance on the National Board of Medical Examiners Neurology Subject Examination and an objective standardized clinical examination (OSCE). They found a significant correlation between the number of outpatient logged and scores on the subject test and written component of the OSCE. These findings contrast with those of Poisson et al.,2 who found no correlation between number of patients logged and final clerkship performance or total written examination scores, and a negative correlation between number of patients seen in diagnostic categories and test disease category subscores.

A few distinctions between these studies might explain these differences, including a more standardized examination and larger patient volume in the current study, where the average number of outpatients logged per student in 1 week was 24.8, compared to 17 in the 4-week clerkship in the previous study. It is tempting to speculate that there may be a threshold number of patients seen before clinical experience outweighs other forms of clerkship learning.

The current study is from a single medical school and only assessed patient experience from one clerkship component. Further multicenter studies are needed to confirm that more—and what kind of—patient encounters are better regarding knowledge and skills gained in a neurology clerkship. Finally, both this study and the study by Poisson et al. used patient logs as a measure of patient encounters; though each came to different conclusions about their effectiveness, neither used a control group without case logs. Even if the intuitive findings from the current study hold up, future studies should also assess whether the specific, time-consuming act of logging patients has any intrinsic value, or lack thereof, in educational outcome.


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From the Department of Neurological Sciences, Rush University Medical Center, Chicago, IL. Study funding: No targeted funding reported.

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clerkship with other inpatient components, our study
does not lend insight into whether a similar correlation
is noted with inpatient volume.

The exploratory analysis evaluating the breadth of
cases students encountered in neurology clinic reveals
exposure to a broad range of clinical symptoms and
disorders. These findings do not reflect the prevalence
of neurologic disorders at the population level but are
likely influenced by a number of factors, including
prevalence of these disorders at an institutional/
departmental level as well as the interest, enthusiasm,
and availability for faculty within specific subspecialties
to provide clinical education to students in the
clinic. Prior evaluation of categories of cases encoun-
tered by students on neurology clerkships employed
different methodology and included inpatient clinical
experiences, making direct comparison difficult.\textsuperscript{5}
Comparison to neurology resident outpatient expo-
sure is also difficult due to similar reasons.\textsuperscript{4,6,7}

Despite the positive aspects of case logs, many
clerkships do not employ them. There is additional
work required of trainees to complete the logs.\textsuperscript{8,9}
The logs rely on student accuracy in recording patient
encounters, which can be underestimated or overesti-
ated. While case logs can be used to tally the types
of patients encountered, they do not reflect the depth
of experience. However, our results demonstrate that
the volume of cases logged is predictive of educational
outcomes on standardized examinations of medical
knowledge. Of potential greater significance is the
relationship between volume of cases logged and skill
in the formulation of a clinical assessment and man-
agement plan. Our ability to evaluate this skill may
provide us with a means to assess individuals as they
progress from trainees to independent clinicians.

AUTHOR CONTRIBUTIONS

Drs. Albert, Bronson, and Lukas contributed to the conceptualization and
design of the work. Drs. Amidei and Lukas performed the statistical analyses.
Drs. Albert, Bronson, Amidei, and Lukas contributed to the analysis and inter-
pretation of the data. Drs. Albert and Lukas contributed to drafting of the
manuscript. Drs. Albert, Bronson, Amidei, and Lukas contributed to revising
the manuscript critically for intellectual content. Drs. Albert, Bronson, Amidei,
and Lukas gave final approval of the version to be published.

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Go to Neurology.org for full disclosures.

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Education Research:
Neurology training reassessed
The 2011 American Academy of Neurology Resident Survey results

ABSTRACT
Objective: To assess the strengths and weaknesses of neurology resident education using survey methodology.
Methods: A 27-question survey was sent to all neurology residents completing residency training in the United States in 2011.
Results: Of eligible respondents, 49.8% of residents returned the survey. Most residents believed previously instituted duty hour restrictions had a positive impact on resident quality of life without impacting patient care. Most residents rated their faculty and clinical didactics favorably. However, many residents reported suboptimal preparation in basic neuroscience and practice management issues. Most residents (71%) noted that the Residency In-service Training Examination (RITE) assisted in self-study. A minority of residents (14%) reported that the RITE scores were used for reasons other than self-study. The vast majority (86%) of residents will enter fellowship training following residency and were satisfied with the fellowship offers they received.
Conclusions: Graduating residents had largely favorable neurology training experiences. Several common deficiencies include education in basic neuroscience and clinical practice management. Importantly, prior changes to duty hours did not negatively affect the resident perception of neurology residency training. Neurology 2012;79:1831-1834.

GLOSSARY
AAN = American Academy of Neurology; ACGME = Accreditation Council for Graduate Medical Education; CNRF = Consortium of Neurology Residents and Fellows; GES = Graduate Education Subcommittee; MRS = member research subcommittee; NCS = nerve conduction studies; RITE = Residency In-service Training Examination.

There have been dramatic changes in neurology residency training. The Accreditation Council for Graduate Medical Education (ACGME) instituted duty hours, restricting residents to 80 hours/week in 2003 with at least 1 day off per week and 12 hours in between shifts. These duty hours were further refined in 2011 with the restriction of postgraduate year–1 shift lengths to less than 16 hours and graduated supervision of middle and senior residents. Residents are also challenged by increased clinical productivity demands. Despite the restricted timeline for training, residents must develop the necessary skills to become proficient in neurology.

The Graduate Education Subcommittee (GES) has been charged by the Workforce Task Force of the American Academy of Neurology (AAN) to evaluate the training residents receive by using a survey every 3 years. This process allows the AAN to receive feedback regarding the quality of the training process and identify deficiencies. The 2008 AAN Resident Survey represented one of the largest efforts to date to assess neurology resident education. Residents assessed the impact of duty hour restrictions, faculty and curriculum quality, and attitudes regarding fellowship training and made specific recommendations based on those data. The current survey assesses the effect of those recommendations and the quality of neurology resident education as perceived by trainees.
METHODS The chair of the Consortium of Neurology Residents and Fellows (CNRF) revised the original 2008 survey created by members of the CNRF and GES. The member research subcommittee (MRS) reviewed the draft prior to distribution.

The target audience was all US adult and child neurology residents who completed training in 2011 (n = 742). Excluded from survey distribution were members not in their first year of training, residents who had received 3 surveys in the past 3 years, officers of the CNRF, and members of the GES and MRS. The survey was distributed in May 2011 via postal mail with a cover letter or e-mail with a link to the online version. Second and third reminders were distributed by postal mail and e-mail. Data collection closed in July 2011. Survey analysis combined adult and child neurology residents. Longitudinal differences between survey responses were tested for significance using Fisher exact test.

RESULTS The survey response rate was 49.8% (308/619). The margin of error for all respondents was 5.4%, 95% confidence level. The average age of the respondents was 33 years and 57.9% of the respondents were male. Differences in age and gender between the survey respondents and nonrespondents were not significant.

Residents were generally satisfied with their training (appendix e-1 on the Neurology® Web site at www.neurology.org). Fifty-nine percent rated their neurology faculty as excellent. The majority of residents believed their programs adequately prepared them in the areas of patient management and differential diagnosis. Both clinical skills training and grand rounds conferences rated very well or well (90% clinical skills training, 83% grand rounds conferences). However, resident endorsement of basic science education was less robust; only 54% rated preparation in basic science as very well or well. The majority of residents were satisfied with research opportunities provided during residency. A minority of residents (28%) reported somewhat well or not well training in subspecialty areas they desired. A review of their comments indicates nerve conduction studies (NCS)/EMG was the most commonly deficient subspecialty area.

The majority of residents did not believe their residency prepared them adequately for practice issues (billing, contracts, malpractice, coding, and office management), with the exception of electronic health records. The majority of residents (67%) supported residency training as the appropriate time to learn this information.

In comparison with the previous survey, all residents who responded to this survey worked under the 2003 duty hours restrictions and prior to the institution of the 2011 duty hour restrictions. The majority of residents responded that patient care and resident education have either been positively impacted or not affected by the changes, while endorsing a positive impact on resident’s quality of life.

A total of 86% of residents intend to pursue fellowship training following residency, split evenly between their current institution and another institution. A total of 81% of these respondents will be pursuing a clinical fellowship. When evaluating how residents chose their fellowship, the 3 top reasons were patient contact, academic environment, and quality of life. Financial reasons and location were less important in residents’ decisions. Most fellowships will be 1 year in duration. Residents were most often guided in their decision by a mentor at their institution. Following fellowship training, 37% plan to enter academic practice, 23% private practice, 7% clinical or basic science research, and 29% are undecided.

The majority of residents (71%) agreed the Residency In-service Training Examination (RITE) assisted them with self-study. A total of 14% of respondents indicated the scores were used as one component of fellowship selection criteria, promotion to the next year of residency training, selection for honors, or for comparison to other residents. The RITE is intended as an educational tool within residency. Other use may qualify as misuse of this examination, specifically use as a certifying or qualifying examination, such as selection of candidates for fellowship positions.

Most foreign medical graduates (79%) intend to stay in the United States following completion of their residency training.

One objective measure of neurology training might be considered ABPN board pass rates. In 2008, adult and child neurology applicants took the same examination, while in 2011 the examinations were separate (table e-1). Overall, neurology residents had a statistically significant decrease in their first and overall pass rates despite similar examination format (ABPN staff, personal communication, 2011).

Similar items between the 2 surveys were analyzed for change. No responses were statistically different except for an increase in the number of residents entering fellowship (p < 0.05) (table 1). Specifically, residents remained satisfied with their clinical training and continued to identify deficiencies in practice issues and basic sciences. A similar percentage of respondents endorsed the RITE as helpful for self-study and reported their scores used for purposes other than self-improvement. There was no change in resident career choices following fellowship training.

DISCUSSION This survey is a longitudinal effort to capture the quality of neurology residency training, assessed by the graduating trainees, and is the largest


<table>
<thead>
<tr>
<th>Response item</th>
<th>2008 survey</th>
<th>2011 survey</th>
<th>p Value of difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respondents</td>
<td>285</td>
<td>308</td>
<td></td>
</tr>
<tr>
<td>Response rate, %</td>
<td>54.5</td>
<td>49.8</td>
<td>0.12</td>
</tr>
<tr>
<td>Entering fellowship, %</td>
<td>77.7</td>
<td>85.6</td>
<td>0.018</td>
</tr>
<tr>
<td>Adequate preparation for patient management*</td>
<td>92.9</td>
<td>93.8</td>
<td>0.741</td>
</tr>
<tr>
<td>Adequate basic science education*</td>
<td>53.2</td>
<td>53.9</td>
<td>0.869</td>
</tr>
<tr>
<td>Quality of neurology faculty</td>
<td>92.3</td>
<td>92.2</td>
<td>1.00</td>
</tr>
<tr>
<td>RITE assists with self-study*</td>
<td>73.2</td>
<td>71.1</td>
<td>0.645</td>
</tr>
<tr>
<td>RITE used for purposes other than self-improvement</td>
<td>14.5</td>
<td>14.2</td>
<td>1.00</td>
</tr>
<tr>
<td>Adequate practice management training*</td>
<td>19.0</td>
<td>23.0</td>
<td>0.150</td>
</tr>
<tr>
<td>Plan to enter private practice after fellowship</td>
<td>28.3</td>
<td>22.6</td>
<td>0.171</td>
</tr>
<tr>
<td>Plan to enter academics after fellowship</td>
<td>32.7</td>
<td>37.4</td>
<td>0.251</td>
</tr>
</tbody>
</table>

Abbreviation: RITE = Residency In-service Training Examination.

* Sum of top 2 response options; either excellent and good, very well and well, or strongly agree and agree.

A minority of residents did not receive the clinical subspecialty training they desired, most commonly EMG, EEG, critical care, and neuro-oncology. Similar concerns were not noted in the 2008 study. The ACGME’s program requirements for neurology mandate certified faculty in all neurology subspecialties be available to neurology residents during their training. Although growth in emerging fields such as neurocritical care may improve educational access to these areas in some programs, deficiencies in exposure to common technical disciplines, such as EEG and NCS/EMG, likely represent programmatic issues within specific residencies. Compliance with these ACGME directives has taken on heightened importance, and the development of formalized reciprocity programs between institutions may become necessary.

A significantly higher fraction of trainees are pursuing subspecialty fellowship training, resulting in a fundamental education shift with fellowship becoming an extension of residency. Internal AAN member data indicate 25% of junior members are fellows. This is notable given the relative lack of attention this group receives by regulatory and specialty organizations. Aside from patient contact and the educational environment of the fellowship, quality of life is the third most common factor in deciding which fellowship to pursue; 50% of respondents indicate quality of life was a very important factor in their fellowship decision. This may influence traditionally underserved subspecialties to tailor their Fellowships to become more competitive. Following fellowship training, more residents express a preference for an academic practice setting than private practice, although 28% were undecided. This preference differs from AAN membership demographics, which report 21% of US neurologists practice in a university setting, and suggests a change in practice preference during fellowship training.

This survey assesses the quality of residency training as perceived by the trainee at the time of completion. There is a paucity of objective measures of residency training quality. One objective measure, neurology certification first-time pass rates are significantly lower in the 2011 group (table c-1) (ABPN staff, personal communication, 2011). This dataset was restricted to the years residents were surveyed, is of unclear significance, and does not necessarily constitute a trend toward lower pass rates. Other potential measures include trainee perception 10 years after completion of residency, which may further inform the perception of strengths and weaknesses. Beyond resident perception, future studies may obtain
the perspective of employers and hospital systems with regard to specific core competency or milestone outcomes.

One potential limitation of this study is the relatively low response rate on both the 2008 and 2011 surveys. This ratio may potentially bias the results toward a subset of residents and may not represent the entire cohort. A second limitation is the combined analysis of adult and child neurology residents. While this provides a global perspective, future surveys ought to include subanalysis of both residencies. Finally, this is an anonymous survey which limits the authors' ability to provide clarification of respondents' answers. It is possible that respondents may interpret questions differently. However, questions provided in 2008 and 2011 were answered similarly, which suggests similar interpretations between different cohorts of residents.

Neurology residents appear satisfied with the structure and quality of their training program. Consistent limitations of training programs include the availability of all subspecialties, education in practice management, and basic neuroscience. Since these same areas were cited as problem areas in the 2008 survey, an innovative approach to addressing these issues will be required. Given the AAN infrastructure already in place, we anticipate transitioning AAN educational programs in basic neuroscience and practice management to an online format as a potential response to these concerns.

AUTHOR CONTRIBUTIONS
Nicholas E. Johnson: drafting manuscript, design of project. Matthew Mace: revision of manuscript, analysis of data. Mary Coleman: design of project, revision of manuscript, analysis of data. Ralph Jozefowicz: design of project, revision of manuscript. John Engstrom: revision of manuscript, analysis of data.

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DISCLOSURE
The authors report 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: Neuropalliative care

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Palliative medicine, as defined by the World Health Organization, is the specialty that recognizes and attempts to prevent or alleviate physical, social, psychological, and spiritual suffering. Understanding the principles of palliative care should be an essential component of neurologic training, as the trajectory of many neurologic illnesses is progressive and incurable. Given the delicate nature of many of the conversations that neurologists have with patients at the time of diagnosis or during acute illness and hospitalization, expertise in discussing a patient's wishes, handling difficult conversations, and providing adequate symptom-based management is critical. Neurologists are often viewed as consulting physicians; however, patients living with chronic neurologic diseases such as multiple sclerosis, dementia, Parkinson disease, amyotrophic lateral sclerosis (ALS), or sequelae of stroke often consider their neurologist as one of their primary physicians. Therefore, neurologists are positioned in both the outpatient and inpatient care settings not only to address symptoms referable to the disease but also to improve overall quality of life for patients and caregivers and to facilitate end-of-life care.

The intersection of neurology and palliative care. For decades, neurologists have acknowledged the importance of offering quality care to dying patients and the need for improved symptomatic management of patients at the end of life. Despite this necessity, widespread incorporation of palliative care into neurologic practice has been limited. Lack of knowledge regarding opioid dosing and titration and uncease with prescribing analgesics are significant barriers. In a study assessing pain medicine education among practicing neurologists, 89% of respondents thought that more pain education was needed in residency training, and 91% of respondents thought that more pain education was necessary for practicing general neurologists. A survey of US neurologists' beliefs and attitudes surrounding end-of-life care indicated that there was a lack of general knowledge regarding basic palliative care principles. The study found that 37% of respondents thought it was illegal to administer analgesics in doses that risked respiratory depression in terminally ill patients with ALS, and 40% of respondents thought that legal counsel was needed to consider withdrawal of life-sustaining treatment.

Efforts to address the palliative care knowledge gap among neurologists have emerged through American Academy of Neurology (AAN) educational programs. Since 1971, sessions focused on pain management have been offered at the annual meetings, and since 2007, palliative care courses have been available to attendees. A wide variety of topics have been covered, including methods of improving mobility in patients with ALS, treatment of nonmotor symptoms in patients with Parkinson disease, and end-of-life care. The AAN also established a Pain and Palliative Care Section in 1996 as a forum for those interested in pain as it relates to terminal and end-of-life conditions.

The Accreditation Council for Graduate Medical Education (ACGME) requires that adult neurology residency training include exposure to end-of-life care and palliative care topics, as well as pain management. Palliative care instruction has been integrated at multiple levels of graduate education. According to a 2009 survey of adult neurology program directors, 52% of programs provide a didactic on end-of-life and palliative care principles. Five percent of programs have an internal rotation, and 87% of programs offer an external rotation in palliative care. In addition to hospital-based rotations and individual didactics, palliative care courses that are geared toward improving resident knowledge in end-of-life care, prognostication, opioid dosing, communicating with patients and their families, delivering bad news, and holding a family conference have been successfully implemented. This method has demonstrated better postcourse knowledge and confidence in performing these tasks.

Postresidency palliative care training. Opportunities for advanced training in palliative medicine are available to interested neurologists. In 2006, Hospice and Palliative Medicine was recognized by the American Board of Psychiatry and Neurology (ABPN) as a subspecialty with a qualifying examination. According to the ABPN Credentials Department, as of March 2013, 53 neurologists are board-certified in palliative medicine, which represents approximately 0.3% of the neurology workforce.

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
Beginning in 2012, a 12-month fellowship training program by a board-eligible or board-certified allopathic physician is required for board certification in Hospice and Palliative Medicine. According to the American Academy of Hospice and Palliative Medicine, fellowship training programs focus on interdisciplinary teamwork, quality improvement, and research methodology in patients with advanced illness; neuropsychiatric and medical comorbidities in populations with life-threatening diseases; the management of pain and nonpain symptoms; ethical and legal decision-making, communication; psychosocial and spiritual issues; death and dying; bereavement support for the family; and the hospice and palliative approach to care. Exposure to long-term, hospice, and inpatient care is also a required part of the training. There are 85 fellowship programs, 78 of which are approved by the ACGME.

In addition to dedicated palliative medicine fellowships, experiential learning may be incorporated into neurology subspecialty postresidency training. Fellowships with patient exposure primarily in the inpatient (i.e., neurohospitalist, neurocritical care) and outpatient (i.e., behavioral neurology, neuromuscular, and movement disorders) setting would benefit from an elective rotation with palliative medicine or hospice. The emergence of simulation centers in academic institutions could be leveraged to develop neurosimulation modules to demonstrate palliative care competency.

Neuropalliative care career opportunities. Although some physicians trained in palliative medicine choose to abandon their primary specialty to concentrate on palliative medicine full-time, most neurologists incorporate the principles into their general or subspecialty practice.

There are opportunities for neurologists to primarily practice palliative care as hospice directors and liaisons, as fellowship program directors, or as consultants on a palliative medicine service. In the future, neurologists trained in palliative care may assume more specialized roles such as performing consultations in the neuroscience intensive care unit, acting as members of institutional ethics committees, providing interdisciplinary care in ALS clinics, or offering neurologic expertise on the inpatient palliative care service.

The value of incorporating a trained neurologist into the multidisciplinary palliative care team is that neurologists would be able to offer disease-specific knowledge, including the typical trajectory and prognosis of common neurologic diseases, as well as anticipatory guidance to facilitate management of typical symptoms that often arise as the disease progresses. In addition, neurologists are adept at interpreting neurologic signs that may be early indicators of disease progression or distress and may incorporate neuroimaging results into discussions with patient families and care teams to further understanding and acceptance of the terminal nature of the disease process. Neurologists would also aid the team in delivering appropriate end-of-life care for patients with catastrophic intracranial processes and in patients who are approaching brain death.

Common scenarios that illustrate the value of neuropalliative care include massive intracranial hemorrhage or malignant cerebral infarction. Although a poor clinical outcome is likely for many patients, some situations present an uncertain prognosis. In these instances, neurologists have an opportunity to serve a pivotal role in leading the conversation regarding the patient’s clinical course. Facilitating discussions with the patient and the family about critical decisions such as whether to withhold or withdraw life-sustaining measures or how long to conduct a timed trial of an intervention may assist the family with making difficult decisions that are aligned with the patient’s overall goals of care. Keeping the neurology team involved during these times of uncertainty encourages continuity of care and builds trust with the patient and the family. Palliative care principles such as addressing the psychological issues that may arise as a result of a physical disability, supporting a new caregiver, managing symptoms, offering spiritual care, and providing care planning resources may be incorporated into these interactions to promote a sense of comprehensive care for the patient.

Neurologists trained in palliative care also have an opportunity to teach neurology trainees how to care for patients across the continuum of their diseases, including how and when to shift the focus of care from disease-specific treatment to focus on symptom control and quality of life and how to engage in delicate conversations about end-of-life care and hospice. The hope is that by increasing the number of neurologists with training in palliative care and end-of-life care, a trend will emerge toward improved symptom management, earlier hospice referrals, and decreased aggressive care at the end of life. Having the dual skill sets of neurology and palliative medicine would prove invaluable to patients, families, and the palliative medicine consult teams.

The future of neuropalliative care. The value of neurologists with advanced training in palliative medicine will likely increase in the near future as measuring end-of-life care evolves into a standardized quality metric in parallel with incentives to decrease hospitalizations and length of stay. In addition, continued scrutiny of health care costs at the end of life will undoubtedly encourage physicians, including neurologists, to focus on advance care planning and symptom control during the earlier stages of chronic illness.

Neuropalliative care is a burgeoning subspecialty benefiting from an increasing interest by recent residency graduates. It has the potential to serve a vital
role in the management of our patients, those with chronic, degenerative, incurable, and end-stage neurologic diseases, as we aim to improve the quality of life for our patients throughout their disease processes while they are living and while they are dying.

AUTHOR CONTRIBUTIONS
M.T.R.: study concept and design, acquisition of data, analysis and interpretation, critical revision of the manuscript for important intellectual content. K.M.B.: analysis and interpretation, critical revision of the manuscript for important intellectual content, study supervision. All authors read and approved the final manuscript.

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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 Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
Emerging Subspecialties in Neurology: Fellowship in experimental therapeutics of neurologic disease

Fellowships in experimental therapeutics are one solution to the challenge of developing the next generation of clinical researchers in the neurologic sciences. Through didactic teaching, mentoring, clinical research experience, hands-on training in trial design and execution, and preparation in grant writing, fellowships in experimental therapeutics prepare new investigators for clinical research careers in academic medicine or industry.

BACKGROUND This is an exciting time in medicine. There are rapid advances in our understanding of pathologic mechanisms of disease, in conjunction with an amazing potential to alter the course of disease by targeting the fundamental molecular changes that cause disease. Advances in treatment are possible in all areas of neurology—from cerebrovascular disease, epilepsy, and neuromuscular disorders, to hereditary and degenerative disorders such as Huntington disease, Parkinson disease, and Alzheimer disease. Clinician scientists are needed to help translate these rapid advances in basic sciences into improvements in patient health.

Even with this unprecedented growth in opportunities, the number of college graduates applying to medical school has been relatively flat, and too few medical graduates pursue a clinical research career. Despite efforts to increase the attractiveness of clinical research by instituting government-funded clinical research training awards, the average age at first independent federal grant (R01) for an MD is 44 years, significantly older than 2 decades before.1,2

Concerns about the dwindling number of physician scientists have led the NIH and Association of American Medical Colleges (AAMC) to develop initiatives to address this gap.3-6 The 2002 NIH Roadmap Initiative aimed to bridge the gap between pathophysiologic advances and clinical care. The AAMC released a report in 2006 calling for medical schools and teaching hospitals to incorporate courses in clinical and translational research into medical student and residency training.7 Ensuring an adequate future workforce is one of the major challenges facing the national clinical research enterprise.2

There are a variety of postresidency training options available for individuals interested in a career in clinical research in the neurologic sciences. Many universities offer Masters of Science in Clinical Research, Masters in Public Health, or certificates of completion. These programs are typically didactic in nature, offering courses in biostatistics, epidemiology, pharmacology, ethics of human research, grant writing, and clinical trial design. The NIH has developed grant programs targeted at individual investigators: the K23/K08 awards are designed to help young investigators early in their career to develop mentored clinical research proposals with the goal of independence; transitional awards such as the K12 program are specifically designed to transition young investigators to a K23, K08, or early R-series award. Many professional organizations and disease foundations offer competitive clinical research training grants which offer salary support and variable amounts of protected time for mentor-driven research projects, typically for 1–2 years. Some examples include the American Academy of Neurology’s Clinical Research Training Fellowship, the Muscular Dystrophy Association’s Clinical Research Training Grant, The Parkinson’s Disease Foundation Fellowship for Clinical Neurologists, and the Epilepsy Foundation’s Research and Training Fellowships for Clinicians.

TRAINING PROGRAMS IN EXPERIMENTAL THERAPEUTICS Experimental therapeutics, the process of translating basic science discoveries into novel therapeutic approaches for patients, is one aspect of clinical research training that has yet to receive much targeted attention in neurology. Experimental therapeutics has long been considered part of training in pharmacology and oncology where there is a postfellowship path for clinical trial training.
State University has a Fellowship in Clinical Pharmacology open to licensed physicians interested in a career in clinical pharmacology and clinical trials (http://www.clinpharm.osu.edu/fellowshipprogram/index.cfm). There are no ACGME-accredited fellowship training programs in experimental therapeutics. The American Academy of Neurology online searchable fellowship directory (http://www.aan.com/education/fellowships/) identifies many programs with experimental therapeutics listed as a primary or secondary topic of the fellowship (table).

Training opportunities outside of degree and fellowship programs also exist in neurology. The National Institute of Neurological Disorders and Stroke–sponsored Clinical Trial Methods Course in Neurology is a 1-week intensive training in core principles of clinical trial design and conduct for fellows and young investigators. The program focuses on mentored development of a clinical trial protocol.

**FELLOWSHIPS IN EXPERIMENTAL THERAPEUTICS IN NEUROLOGY** Two experimental therapeutics training programs in neurology serve as complementary models for future clinical research training programs. The University of Rochester Medical Center’s Fellowship in Experimental Therapeutics of Neurological Diseases (URMC Program, http://www.urmc.rochester.edu/neurology/training/experimental-therapeutics.cfm) trains fellows for careers as clinical neuroscientists involved in both clinical and translational research. The UCB Fellowship in Neurology and Clinical Drug Development represents a collaboration between UCB Biosciences, University of North Carolina Eshelman School of Pharmacy, Duke University, and the Hamner Institutes for Health Sciences (UCB program, http://www.pharmacy.unc.edu/programs/fellowships/ucb-fellowship-in-neurology-and-clinical-drug-development) and prepares fellows for careers in pharmaceutical medicine. Both programs are postresidency training for MDs or MD, PhDs who have completed their training in internal medicine or pediatrics and clinical neurosciences. The UCB program accepts 1 fellow per year for 2 years of training. The URMC program accepts 2–4 trainees per year for periods of 2–3 years. Fellows are trained in the design, implementation, analysis, reporting, and ethics of clinical trials, cost-benefit analysis, and outcomes research.

Both programs provide both preceptorial and didactic teaching, but with slightly different emphasis. In both programs fellows participate in coursework in biostatistics, data analysis and computing, and ethics in research, which can be expanded into a formal Master’s degree program (MPH, MS-CI, MS-Tr). The UCB program has a larger emphasis on pharmacology, with courses in pharmacokinetics, dynamics, or genetics, and molecular biology and drug metabolism. The URMC program has developed 3 seminar programs to complement formal coursework: 1) Working Group on Clinical Trials, 2) Mechanisms of Disease and Therapeutic Development Workshop, and 3) Mellow Fellows. The twice-monthly Working Group Seminars provide an interactive forum for Neurology, Biostatistics, and Community and Preventive Medicine junior and senior faculty to discuss planned or in progress clinical trials, pilot data, and ideas for future studies. This forum is complemented by Mellow Fellows, an informal research-social meeting held monthly designed to provide fellows an opportunity to brainstorm new ideas with experienced investigators, biostatisticians, and each other. The Mechanisms of Disease Workshop focuses on the molecular underpinnings and basic science advances that may lead to therapeutic interventions.

<table>
<thead>
<tr>
<th>Table</th>
<th>Fellowships in neurology offering experimental therapeutics training*</th>
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<tr>
<td>Primary topic</td>
<td>Institution name</td>
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<tr>
<td>AIDS</td>
<td>Beth Israel Deaconess Medical Center</td>
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<td>Autonomic disorders</td>
<td>Clinical Neurocardiology Section, DIR, NINDS, NIH</td>
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<tr>
<td>Basic research</td>
<td>UMDNJ-New Jersey Medical School</td>
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<td>Behavioral neurology</td>
<td>University of Rochester</td>
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<td>Cerebrovascular disease/stroke</td>
<td>University of Rochester Medical Center</td>
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<td>Epilepsy</td>
<td>Medical University of South Carolina</td>
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<td>Epilepsy</td>
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<td>Memory disorders</td>
<td>University of Alabama at Birmingham</td>
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<tr>
<td>Movement disorders</td>
<td>University of Rochester Medical Center</td>
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<tr>
<td>Movement disorders</td>
<td>Duke University Medical Center</td>
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<td>Movement disorders</td>
<td>Johns Hopkins School of Medicine</td>
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<td>Movement disorders</td>
<td>Rush University Medical Center</td>
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<td>Movement disorders</td>
<td>Oregon Health Sciences University &amp; Portland VA Medical Center</td>
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<td>Movement disorders</td>
<td>Medical College of Georgia</td>
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<td>Movement disorders</td>
<td>The University of Maryland</td>
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<td>Movement disorders</td>
<td>Cleveland Clinic Foundation</td>
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<td>Massachusetts General Hospital</td>
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<td>Movement disorders</td>
<td>Columbia University Medical Center</td>
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<td>Movement disorders</td>
<td>University of Chicago</td>
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<td>Movement disorders</td>
<td>University of Florida Center for Movement Disorders and Neurorestoration-McKnight Brain Institute</td>
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<tr>
<td>Movement disorders</td>
<td>Baylor College of Medicine</td>
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<tr>
<td>Multiple sclerosis</td>
<td>University of Rochester Medical Center</td>
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<tr>
<td>Neuro-ophthalmology</td>
<td>University of Rochester</td>
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<tr>
<td>Neuromuscular disorders</td>
<td>University of Rochester Medical Center</td>
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* Data compiled from AAN Fellowship online directory.
Both programs are flexible and tailored to a great degree on the needs of the fellow. In both programs the first year is largely comprised of coursework and designing and implementing fellow-initiated research projects.

During the first year fellows in the UCB program participate in brief exposures to various aspects of drug development at UCB Biosciences complemented by fellow-initiated research projects at Duke, UNC, or the Hamner. The UCB Biosciences experience expands to an intensive (4 days/week), hands-on participation in all aspects of drug development during the second year. This directly builds upon core knowledge in developing, reviewing, and composing protocols and regulatory submissions, and fellows magnify understanding of the process of execution of phase I–III clinical trials, including site selection, start-up, and monitoring, as well as issues of human subjects protection and recruitment.

The heart of the URMC program is its formal one-on-one mentoring program. The preceptorial team always includes a clinical neuroscientist and biostatistician. A basic neuroscientist and other clinical neuroscientists are often involved. The trainee and mentors work together to develop a long-term plan for training that includes development of one or more hypothesis-driven clinical research projects. The team meets regularly, typically on a weekly basis, to review and discuss the progress of the project. As it is not typically feasible to conceive, develop, and execute a clinical trial from beginning to completion during the fellowship period, each trainee is invited to participate in ongoing clinical trials at various stages of execution in order to directly learn about the process of drug development. Trainee roles have included medical monitor, steering committee member, subinvestigator, and writing group member, among others. Direct experience is a critical component of the educational program.

**TRACK RECORD** Programs such as the UCB program and URMC program have served as a launching pad for careers in academic medicine focused on experimental therapeutics. From URMC's 48 past trainees alone, graduates have acquired over 70 extramural grants, including 17 NIH R award and 15 NIH K awardees.

**DISCUSSION** There are many options open to the postresidency neurologist interested in clinical research. These include federally funded competitive programs, masters programs in clinical or translational research, and grants funded through subspecialty or professional organizations. Many fellowships offer training in a variety of aspects of clinical research as part of their subspecialty training. The URMC program and UCB program are 2 of a growing number of programs that focus on experimental therapeutics and opportunities for direct clinical trial experience. Trainees spend the majority of the fellowship program either working directly with industry or paired with a mentor with experience in their field of interest. This opportunity combined with didactic fundamentals and the skill set for securing funding prepares new investigators for an academic career in clinical neuroscience.

**AUTHOR CONTRIBUTIONS**

J. Statland: drafting/revising the manuscript, acquisition of data. R. Griggs: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, study supervision, obtaining funding. E. Augustine: drafting/revising the manuscript, study concept or design, analysis or interpretation of data.

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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: Acute ischemic stroke
An international experience

Mr. Q, a 72-year-old right-handed man with hypertension, hyperlipidemia, recurrent angina, and a 30 pack-year smoking history, is a retired scientist living in the United States with his wife. He recently visited his native country, Ukraine, for the first time in almost 30 years. After an emotional day with family members, he returned home and suddenly became diaphoretic and weak, and ultimately lost consciousness. His wife drove him to the nearest open medical clinic. Because it was severely undersourced, he was then emergently taken by ambulance to a larger hospital 6 hours away. He regained consciousness by the time he arrived at this second hospital. After he was examined, his wife was told that, as a consequence of an acute stroke, her husband would no longer be able to move the left side of his body or produce speech. The physician explained that nothing could be done because the pharmacy was closed and that Mr. Q might not survive. His wife insisted that she could “pay with dollars” and that the pharmacy be opened. The physician then provided her with a list of 3 medications, which she obtained at this pharmacy (after it opened at her insistence) and swiftly brought back to the hospital. She described how her husband received a yellow powder that was then mixed in saline and administered IV. The second and third medications were clear liquids delivered IV and subcutaneously, respectively. Mr. Q also received IV fluids, and over the next 2 hours, the patient’s strength and language functions recovered to baseline. He continued to receive care at this hospital and received his first head CT scan on his fourth hospital day. Upon discharge, he and his wife quickly flew back to the United States.

Mr. and Mrs. Q presented to our emergency room the following day. Armed with a file of hospital documents in Ukrainian and a compact disc containing his CT scan, Mrs. Q eloquently described the recent turn of events. She was particularly upset and embarrassed by the quality of care that her husband had received back home. Mr. Q’s neurologic examination was completely normal. We were able to view his original CT scan (figure, A), and identified at least 3 hypodensities suggestive of prior stroke. Concerned that his stroke workup was incomplete, we admitted him to our inpatient service. MRI confirmed that he had indeed sustained an acute infarction of the left posterior inferior cerebellar artery territory just a few days prior (figure, B), and a CT angiogram demonstrated an occluded basilar artery, with a robust collateral system indicative of a chronic occlusion (figure, C). Outpatient Holter monitoring identified numerous episodes of paroxysmal atrial fibrillation, and the patient was started on warfarin.

Mr. Q’s story exemplifies a crisis in international stroke care. Many economically advantaged regions of the world such as the United States have stroke protocols, with access to rapid CTs and tissue plasminogen activator (tPA) readily available. In these regions, academic medical centers are also furnished with stroke units, staffed by skilled nurses who specialize in the care of this patient population. These health care services are not available globally, particularly in nations where the incidence of stroke is increasing. While there has been a 42% reduction in stroke incidence in high-income countries over the past 4 decades, there has been a greater than 2-fold increase in the incidence rates of stroke in low- to middle-income countries.1 The increased incidence may be partially explained by changes in the epidemiology of traditional stroke risk factors, such as in the case of sub-Saharan Africa, where stroke caused by hypertension is now a major cause of premature death.2 Rates of stroke-associated disability and mortality are highest in those countries with the lowest national income, with mortality decreasing by 4% for every additional US $1,000 in per-capita gross national income.3 Developing countries with lower incomes will continue to bear a disproportionately greater fraction of the global burden of stroke as long as the complicated barriers contributing to these disparities remain poorly addressed. Poor public awareness of the symptoms of stroke and the importance of the time window for acute therapy are critical “prehospital” barriers. Poor infrastructure also contributes, because patient transportation systems are often limited and functional CT scanners unavailable or only available on select days of the week. Financial barriers

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therapy to private sector hospitals. These problems support the need for a global endeavor to aggressively address stroke risk factors in low- to middle-income countries as well as to identify funding sources to overcome these barriers to providing rapid stroke care.

What were those 3 medications that Mrs. Q had heroically acquired? Given the speed of his recovery, we wondered whether he had received tPA, and perhaps an IV antihypertensive agent and/or mannitol. On our request, Mrs. Q provided us with that very sheet of paper that contained the 3 drugs inscribed in a foreign script. We were quite surprised to learn that the 3 medications were in fact dexamethasone, citicoline, and L-lysine ascorbate. Despite its known effects in ameliorating cerebral edema, clinical studies conducted before the 1980s demonstrated dexamethasone’s lack of efficacy in the treatment of acute ischemic stroke (particularly among patients with a depressed level of consciousness). These publications uniformly used small, poorly randomized cohorts of patients, and were conducted at a time when CSF analysis was needed to distinguish between ischemic and hemorrhagic stroke. There have been no newer large randomized studies examining the role of dexamethasone in acute ischemic stroke. Citicoline is an exogenously administered form of a membrane phospholipid precursor that showed promising effects in preclinical testing, but failed to show significant benefits in a recent large multicenter randomized controlled trial. However, like most modern neuroprotectant trials, this study enrolled patients that presented to “stroke centers” with well-equipped emergency departments and almost half of these patients received tPA, a scenario vastly different from Mr. Q’s experience. L-Lysine ascorbate is commercially available in some countries as a medication to combat edema, but there are no English-language publications on the use of this medication in acute stroke. Finally, Mr. Q was treated with IV fluids. We were not able to find any trials examining the role of IV fluids in the treatment of acute ischemic stroke. However, a number of retrospective studies have demonstrated that patients with TIIAs or strokes display a high incidence of dehydration (as measured by plasma osmolality), and that this is exacerbated by diuretic intake and dysphagia, and leads to poorer outcome, suggesting that at least a proportion of patients with acute ischemic stroke may benefit from volume repletion.

While Mrs. Q was thankful for our efforts to shed light on the recent turn of events, she was a little upset to learn that we would not continue to administer these 3 medications to her husband to prevent future strokes. Fortunately for Mr. Q, he had experienced a good outcome and was able to travel back to the
United States and receive follow-up care. Our team
spent time reflecting on how we would react if a loved
one was to experience a stroke in a similar setting.
Neuroimaging results several days later confirmed
the presence of a large cerebellar ischemic stroke
without any associated hemorrhage. However, because of
the unavailability of a CT scanner at the time of his
initial presentation, Mr. Q’s physicians could not
have ruled out a hemorrhagic stroke, and tPA would
have been contraindicated. Thus, if citalopram or dex-
amethasone was all that was available, would we also
insist on administering these medications emergently?

While efforts to overcome socioeconomic and edu-
cational barriers to appropriate tPA use are paramount,
these efforts are futile and inapt for countries where
the safe storage and use of tPA remains prohibitively
expensive. Instead, our efforts should focus on stroke
prevention as a more cost-effective means to address
global disparities in stroke disability and mortality,
particularly with regard to addressing hypertension.10
In conjunction with these preventative strategies, we
should develop the means to provide standardized
high-quality acute stroke care in technologically under-
developed settings using cheap treatment strategies.
Our case also suggests the need to reevaluate the effi-
cacy of previously studied neuroprotective therapies,
specifically in rural regions of the world, where their
relative benefit may be the greatest.

AUTHOR CONTRIBUTIONS
Meaghna Colling: drafting/revising the manuscript, study concept or
design, analysis or interpretation of data, accepts responsibility for con-
duct of research and will give final approval. Vasileios-Armenios Lioutas:
drafting/revising the manuscript, study concept or design, accepts respon-
sibility for conduct of research and will give final approval, study super-
vision. Vaishnav Krishnam: drafting/revising the manuscript, accepts
responsibility for conduct of research and will give final approval.

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International Education Issues: Neurology and poverty

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Few people in the world today are rich; the vast majority, 86% of the global population, live in the developing world, in countries that are classified as low or middle income. The most recent data on extreme poverty suggest that nearly a billion people, spread over many continents, live on less than one dollar per day. It is in low and middle income (LAMI) countries where most cases of neurologic disease occur, including stroke, epilepsy, primary headache disorders, and Alzheimer disease, and in these countries neurologic disease is studied little if at all.

The public health challenges for neurologic disorders in LAMI countries are multiple. Among the poor, there is special consideration of the 1) overall burden of neurologic disease, 2) lack of access to essential medications, 3) paucity of epidemiologic research available, 4) reduced ratio of practitioners in LAMI countries, 5) double burden of communicable and noncommunicable disease, and 6) stigma. At every level of society, there is a need for more education, in rich countries as well as poor ones. Health care workers, students, governments, teachers, and members of the general public all have important roles to play.

THE OVERALL BURDEN OF NEUROLOGIC DISEASE Dementia and stroke are among the most common disabling diseases worldwide, and in some regions of the world, stroke accounts for more deaths than ischemic heart disease. Although often considered developed world diseases, 86% of all stroke mortality and 85% of all cases of epilepsy occur in the developing world. Overall, neurologic disorders now account for a greater burden of disease than HIV/AIDS.

LACK OF ACCESS TO ESSENTIAL MEDICATIONS Studies from LAMI countries reveal poor access to underprescribed and often unaffordable medications. In one recent analysis of four low and six middle income countries, just 71.5% of patients with cerebrovascular disease were taking aspirin. In sub-Saharan African nations, most medications are simply not available in public and private facilities, regardless of a patient’s wealth. The World Health Organization (WHO) estimates that 150 countries do not have adequate access to medications to treat pain.

Moreover, 50 to 90% of people in LAMI countries must pay for their medications entirely by themselves. In Chad, a 30-day supply of carbamazepine 200 mg twice daily costs the equivalent of 8.8 days of an unskilled government laborer’s wages, rendering treatment of a very treatable disease effectively unattainable. Thus, access to essential medications is a result of both availability and affordability. Although costs and wages are objectively measured, the health-care seeking behavior of the poor is largely unstudied.

PAUCITY OF EPIDEMIOLOGIC DATA AVAILABLE ON NEUROLOGIC DISEASE From a public health stance, there is a lack of research in neurologic disorders. In other medical specialties, high income countries produce more than 90% of the world’s research although they account for approximately 10% of the global population. This is the so-called 10–90 divide in medical publication. It is uncertain whether the 10–90 divide exists in the neurologic literature because it has not been formally studied except in the case of dementia.

Among the neurologic disorders, research in LAMI countries has been so limited that their prevalence is difficult to estimate. Unlike census reports and sophisticated database analyses available from high income countries, epidemiologic information from LAMI countries is often obtained via tedious door-to-door surveys and reported in non-indexed, low-impact journals. Many studies piggyback on cardiovascular disease research and lack an emphasis on neurologic disorders. Little, if any, is known about the cognitive effects of neuroAIDS outside of industrialized nations.

The value of research publications in LAMI countries also differs. A publication in the devel-
oping world, even more so than in the developed world, may have little effect on real life practice.\cite{12} Thus, searches for “neurology,” “headache,” “dementia,” and other common diseases in popular medical databases reveal no articles on neurologic disease, at any point in time, from a number of LAMI countries, accounting for knowledge gaps that encompass millions of people over decades.

REDUCED RATIO OF PRACTITIONERS IN LAMI COUNTRIES Where neurologists are needed most, they are least likely to be found. Although the WHO estimates that one neurologist is needed for a population of 100,000 people,\cite{13} in Africa, there are an estimated 0.3 neurologists per million.\cite{14} Many countries see neurologic care provided, if at all, by health care workers with no formal training in neurology. Eleven African countries have no neurologists.\cite{15} Physicians practicing in countries with the greatest need of neurologic care lack resources, educational opportunities, and health care workers. Some physicians emigrate to countries that can provide these desired resources and opportunities. An estimated 20,000 physicians leave Africa each year,\cite{16} a region which exemplifies this problem. Compared to the number of physicians who leave, the number of high-income country physicians working in Africa is small.

THE DOUBLE BURDEN OF DISEASE LAMI countries may continue to deal with diseases that have been eradicated or are easily prevented in high-income nations, the so-called double burden of communicable and noncommunicable disease. For example, the last case of locally acquired poliomyelitis occurred in the United States in 1979. Yet needless suffering from poliomyelitis among the poor of Pakistan, Afghanistan, India, and Nepal persists,\cite{17} for both medical and cultural reasons, in a world that has largely moved on.

STIGMA The majority of people with epilepsy, approximately 40 million, do not receive treatment.\cite{1} It would be wrong to assume that this is simply a financial issue, easily corrected by free medications and more health care workers. Recognition of neurologic disorders, particularly neuropsychiatric manifestations, as disease is long overdue.

Adding insult to injury, neurologic disease, even in the richest nations, in the hallways of the wealthiest institutions, can be stigmatized as incurable or barely treatable. In the developed world, common neurologic disorders are both under-recognized and undertreated.\cite{2} Not only a matter of science, this is a failure of education as well. The situation is probably worse in LAMI countries. If such stigmas persist, neurologic disorders will remain distant from the priorities of public health and public policy worldwide.

Conceptually, neurologic disease and poverty are connected. The idea that poverty and its consequences—most notably, malnutrition—can lead to poor cognitive ability, poor school performance, and eventual school desertion has been explored for decades.\cite{18,20} More recently, data from these same countries demonstrate that secondary prevention of neurologic disease in adulthood, such as stroke, is positively influenced by a higher level of education.\cite{21}

Thus, when a neurologic problem is addressed scientifically, it next demands collective action for sustained population-wide health improvement. Although small in scope compared to the burden with which they are faced, a number of agencies, academic groups, and nonprofit organizations have begun the great deal of work required. Solutions occur at multiple levels. In February 2007, the World Health Organization (WHO) and World Federation of Neurology (WFN) addressed the European Parliament, launching Neurological Disorders, Public Health Challenges,\cite{3} a comprehensive summary of the public health knowledge of neurologic disorders to date. Widespread changes for success include the entrance of women into the health care workforce, a focus on neurology within existing health systems, and the need for better epidemiologic information on which to set future priorities. The WHO calls for a “paradigm shift beyond the current preoccupation with prevention and simple curative interventions to encompass long-term support and chronic disease management.”

Others have responded similarly in magnitude. Among them, the Global Campaign Against Epilepsy, the 10/66 Dementia Research Group, the Global Burden to Reduce the Campaign Against Headache, and the WFN have each made progress. The WFN features an online book, Where there is no neurologist,\cite{22} which is meant to act as a guide to para-medical professionals in the care of neurologic disease. Many universities actively organize, sponsor, and encourage their staff and students to train abroad for short periods of time. Most journals, including this one, are available to physicians in low income countries at a reduced rate of subscription. Headache clinics and neurology training programs now exist where previously there have been none. In more
than 100 countries, neurologists and non-neurologists alike participate jointly in alleviating the global burden of neurologic disease.

In the current Resident & Fellow pages of Neurology®, two American physicians recount their experiences studying neurology abroad. Dr. Chad Heatwole, a neurology resident at the University of Rochester, relates his story teaching neurology at Jagiellonian University in Kraków, Poland. Dr. Porter provides an eye-opening account of the neurologic care in an impoverished Kenyan town. Together, their stories provide the humanitarian perspective, inarguably the most important reason of all, to aggressively tackle these challenges.

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This R&F Highlights Booklet is also available in PDF format on the iPad® and mobile versions of Neurology!
**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:
Comparison of symptomatic and asymptomatic persons with Alzheimer disease neuropathology

Jared R. Brosch, MD, MSc
Brandy R. Matthews, MD

Advances in neuroimaging, biomarkers, and clinical data have led to the hypothesis that the pathologic process of Alzheimer dementia begins decades prior to functional decline and diagnosis. High-profile clinical trial results have shown that biomarker changes can be made via pharmacologic intervention; however, the timing of this intervention has likely been too late to affect the cascade of neurodegenerative changes.

In “Comparison of symptomatic and asymptomatic persons with Alzheimer disease neuropathology” by Monsell et al., neuropathologic and clinical data were used to determine the risk of developing clinically significant cognitive impairment. This work represents a significant contribution because it examines a large cohort of autopsy data, which includes patients with Alzheimer dementia neuropathology who were clinically normal or diagnosed with mild cognitive impairment and Alzheimer-type dementia. The authors report a 3-fold increase in the risk of cognitive symptoms in association with quantifiable increases in neurofibrillary tangle pathology. In addition, several other factors, including APOE gene status, history of depression, and age, affect the clinical presentation. The ultimate goal of this investigation and similar studies is to facilitate the early and accurate identification of those at risk of developing Alzheimer dementia such that potentially disease-modifying therapies may be considered.

HYPOTHESIS AND DESIGN The authors hypothesized that there may be specific demographic, clinical, or neuropathologic features that are associated with clinical impairment consistent with a diagnosis of Alzheimer dementia in a group of patients with known Alzheimer dementia neuropathology at autopsy. The study design is case-control with symptomatic dementia as the disease state of interest.

METHODS The data used for this study were extracted from the National Alzheimer’s Coordinating Center Uniform Data Set and Neuropathology Data Set, which included 1,775 patients who underwent autopsy from 2005 to 2012. Only patients who had a clinical follow-up visit to one of the database centers in the year prior to death were included. Other inclusion criteria required the presence of both diffuse plaques and neuritic plaques on pathologic examination. This is important because it excluded subjects with no Alzheimer dementia pathology and also created a “control” group that was asymptomatic clinically yet had neuropathologic changes consistent with Alzheimer dementia. These parameters yielded 906 patients. This approach was derived from the National Institute on Aging–Alzheimer’s Association (NIA-AA) guidelines for the neuropathologic assessment of Alzheimer dementia, which propose the grading of Alzheimer dementia into 4 ranges (not, low, intermediate, high) based on the “ABC” score (A: Thal phase for Aβ amyloid plaques; B: Braak stage for neurofibrillary tangles; and C: Consortium to Establish a Registry for Alzheimer’s Disease neuritic plaque frequency). Notably, Thal phase (the anatomical distribution of amyloid plaques) was not available in the datasets used for this study; however, the inclusion criteria were designed to permit analysis of the largest number of subjects with Alzheimer disease (AD) pathology, given this limitation.

The determination of symptomatic disease was based on the Clinical Dementia Rating scale (CDR), a validated tool that evaluates 6 functional domains and categorizes subjects’ dementia as none, questionable/very mild, mild, moderate, or severe. In this study, any classification greater than “none” (CDR ≥ 0.5) was considered symptomatic. The degree of pathologic changes and other clinical characteristics were then evaluated using logistic regression models (first bivariate, then multivariate) to look for associations with the clinical symptomatology. The results of these analyses are the odds ratios (ORs) of factors that lead to clinically symptomatic dementia based on a cohort of patients with neuropathologic changes consistent with Alzheimer dementia.

RESULTS Demographic data reveal that the cohort was 95% white, 45% female, 41% aged 80–89 years, 70% college-educated, and 45% had at least 1 APOE ε4 allele. The asymptomatic group included 82
subjects, which represents only 9% of the total. The authors point out that the asymptomatic population is slightly older (mean 86.2 years vs 81.3). Also, 52.2% of symptomatic patients had at least 1 APOE ε4 allele, compared to 16.2% of the asymptomatic group. Neuropathologically, asymptomatic individuals were more likely to have low B (neurofibrillary tangles) and low C (neuritic plaques) scores (77%), and 50% of the symptomatic group had both high B and high C scores. In multivariate logistic regression, the only factors that reached statistical significance in asymptomatic subjects were older age, lower Hachinski ischemic score, lack of APOE ε4 allele, and lower B score.

INTERPRETATION The authors sought to elucidate risk factors that were associated with clinically symptomatic Alzheimer dementia in those with known Alzheimer dementia pathology. The design of this work in the form of a case-control study is appropriate to address the authors' goals. Ideally the question that the authors pose would be addressed by a prospective cohort study, which follows patients from asymptomatic enrollment until death; however, the logistics and timing of such a study would likely be prohibitive at present. One of the primary strengths of the study is the number of patients with identified Alzheimer dementia pathology via the current diagnostic gold standard, postmortem neuropathologic examination. However, the number of patients should be considered in the context of an expected effect size for this study, which was not reported. The weaknesses of the study lie mainly in limitations of the available dataset. First, attempting to apply the NIA-AA guidelines to the data is not perfect, as a Thal phase for Aβ plaques was not available. According to the guidelines, the simplest way to include all patients with Alzheimer dementia pathology is to include all patients with at least Thal phase 1 (i.e., an ABC score of 1, X, X eliminates all “no” Alzheimer dementia neuropathology). The C score of 1 or higher used in this study (i.e., requiring the presence of neuritic plaques) may have excluded some patients who would have otherwise met criteria. Due to the limitations in the assessment of diffuse plaques (and missing data in this study), the scheme used by the authors likely led to the most accurate classification possible. Amyloid imaging techniques represent an emerging technology for classifying patients with Alzheimer disease (AD) pathology and may be useful for assigning Thal phase in vivo in future prospective studies.

Another major limitation of the dataset is the small “control” group, with only 9% of patients in the asymptomatic group. One possible explanation for this disparity in group sizes is a sampling bias in which patients with clinical symptoms may be more likely to consent to autopsy and to participate in AD research. Based on current hypotheses of disease progression in Alzheimer dementia and accumulating evidence of neuropathologic changes preceding symptom onset, the predicted proportion of asymptomatic subjects with Alzheimer dementia pathology would be much higher than reported in this study. Another challenge in interpreting these data is the oversimplified classification scheme of symptomatic vs asymptomatic using the CDR. Categorization via the 5 stages of the CDR or use of the CDR sum of boxes score, as opposed to a binary classification, may have been a more clinically relevant assessment of degree of impairment to correlate with risk factors.

The results of this study are presented as ORs, which can be more difficult to interpret compared to relative risk; however, ORs allow for easier adjustment of potentially confounding covariates. Vascular pathology represents a known confounding and contributing factor in the diagnosis of Alzheimer dementia. The investigators did attempt to address this complex issue by pathologically identifying the presence of large and small infarcts as well as amyloid angiopathy. In addition, the Hachinski ischemic score (HIS) was available for 79% of the cohort. In multivariate analysis, only the HIS was correlated with symptomatic Alzheimer dementia, highlighting the relationship between Alzheimer dementia and vascular pathology and the clinical significance of attending to modifiable cerebrovascular risk factors in attempts to maintain brain health.

A seemingly paradoxical observation was that older age correlated with lower risk of symptomatic disease. As the authors suggest, this finding may be the result of a healthy survivor effect and a selection bias of the control group, as persons with memory concerns or a family history of Alzheimer dementia are often compelled to enroll as normal control subjects.

Overall, the authors were able to identify several factors that were statistically significant in predicting the presence of symptomatic disease. Of particular interest, APOE ε4 is strongly associated with symptomatic disease even when adjustments have been made for the underlying neuropathologic changes. One could argue that based on the results of this article, APOE ε4 and the Hachinski score are relatively easily obtained and may aid in the prediction of risk for developing symptomatic AD. Likewise, the importance of neurofibrillary tangles in the development of symptomatic disease is emphasized in this neuropathologic study and consistent with previous reports. Development of imaging techniques specific to neurofibrillary tangles to complement currently available amyloid imaging techniques may also greatly improve the accuracy of prediction of symptomatic AD.
AUTHOR CONTRIBUTIONS
Dr. Bross prepared the original and revised manuscripts. Dr. Matthews edited the manuscript for content and style.

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Journal Club:
Early stroke risk and ABCD2 score performance in tissue vs time-defined TIA

In this journal club article, we evaluate a study by Giles and colleagues\(^1\) that reports stroke risk in patients with classically defined TIA subcategorized by presence or absence of radiologic brain infarction.

The concept of a TIA is evolving in parallel with better understanding of brain ischemia and insights gained from neuroimaging studies. TIAs were classically defined as a sudden focal neurologic deficit resulting from brain or retinal ischemia lasting less than 24 hours.\(^2,3\) The time threshold of 24 hours was arbitrarily chosen, and given that there is no evidence to support any single time criterion associated with infarction, this has appropriately been questioned.

A newer and well-received definition of TIA is "a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction."\(^4\) This definition communicates the important concept that transient symptoms can nonetheless be associated with permanent brain injury, encourages the use of neuroimaging studies, and may promote rapid interventions for acute brain ischemia.

The ABCD2 score, a risk-stratifying score for patients with TIA, is derived from the patient’s age, blood pressure, clinical features, TIA duration, and history of diabetes. This simple, validated score identifies patients at higher risk of early stroke after TIA.\(^5\) Scores are commonly divided into low risk (0–3), intermediate risk (4–5), and high risk.\(^6,7\)

The clinical ABCD2 scale is integrated in this study with results from acute brain imaging to assess how the new tissue-based definition of TIA further assists with risk stratification of patients with transient neurologic symptoms.

HYPOTHESIS AND DESIGN In this analysis of data pooled from 12 medical centers which included 4,574 patients, Giles and colleagues subcategorized TIA as "tissue positive" or "tissue negative," depending on the presence or absence of radiographic brain infarction seen on MRI or CT scans.\(^1\) They set out to determine the added value of brain imaging to the risk stratification of patients with TIA and hypothesized that the ABCD2 score retains its prognostic value within these groups.

These questions are undoubtedly relevant to today’s clinical practice in which imaging studies are increasingly obtained and criteria for admission to the hospital are becoming stricter. Having objective, accurate means of identifying the patients at highest risk for stroke after TIA could facilitate rapid interventions and hopefully lead to better clinical outcomes.

METHODS The authors performed a systematic review of the literature in 2009 and identified 12 research centers that had sufficient prospective data of interest available. To be included, the center needed to have a cohort of patients with TIA (traditional time-based definition), ABCD2 scores, brain imaging, and clinical follow-up until at least 7 days after the TIA. Five studies were based in emergency departments, 5 in specialized neurovascular units, and 2 were population-based. ABCD2 scores were calculated by local investigators and the presence of brain infarction could be determined by a routine report from individual centers. For patients who had MRI with diffusion-weighted imaging (DWI), any acute infarct was counted as tissue-positive (whether or not the location corresponded to clinical symptoms) and for patients with CT, any infarct, regardless of age, was also considered positive. Because CT is less sensitive than MRI for the detection of acute ischemia, combining results from these different imaging modalities could potentially jeopardize the internal validity of the study results. However, this also allows the results to be generalized to a greater extent, given that CT scans are still used as the primary imaging modality for TIA evaluations at some centers.

The statistical method used to determine the predictive power of the ABCD2 score was the area under the receiver operating characteristic curve (AUC). The receiver operating characteristic curve is a graph of sensitivity against 1 – specificity\(^6\) (figure).
The closer the AUC is to 1, the better the test's sensitivity and specificity. An AUC of 0.5, which appears as a straight diagonal line, indicates that the variable has no diagnostic capability.

Of note, the authors did not state the statistical test used for the comparison of the tissue-positive and tissue-negative groups, though based on the nonoverlapping confidence intervals and the p values reported, the comparisons are statistically significant.

RESULTS The authors confirmed that radiographic evidence of brain infarction in patients with TIA is a predictor of higher risk of early stroke. There was a remarkable 18-fold increase in the rate of stroke at 7 days, from 0.4% in those with negative DWI to 7% in those with positive DWI. For those with infarcts on CT scans, the 7-day risk was 3% in those with negative CT and 13% with a positive CT. The overall risk of stroke at 90 days was 2.2% in the tissue-negative group and 12% in the tissue-positive group.

However, the value of brain imaging in addition to ABCD2 score seemed to be less clear when looking at the longer-term outcome of stroke within 90 days, specifically for low-risk patients as stratified by ABCD2 score. Of patients with ABCD2 score ≤3, only 21 patients (2%) had a stroke within 90 days, but over half of these (n = 12, 57%) had tissue-negative imaging.

Nevertheless, the ABCD2 score was predictive of recurrent stroke at 7 days within both the tissue-positive and tissue-negative groups. Of 1,665 patients with ABCD2 ≤3, 10 patients (0.6%) had a recurrent stroke in 7 days, of which 7 were in the tissue-positive group. Of 2,909 patients with ABCD2 ≥4, 135 patients, or 4.6%, had recurrent stroke at 7 days. Ninety-eight of these (73%) had evidence of brain infarction on either MRI or CT.

The AUC for prediction of stroke by ABCD2 at 90 days was 0.66 for tissue-positive and 0.69 for tissue-negative patients. AUC for the prediction of stroke at 7 days was 0.68 for tissue-positive vs 0.73 for tissue-negative. Thus the ABCD2 score meaningfully stratifies risk among both the tissue-positive and tissue-negative groups.

INTERPRETATION In their large, international multicenter study, Giles and colleagues show that the ABCD2 score retains its prognostic value for refining the risk of stroke in both tissue-positive and tissue-negative groups. They also confirm that brain imaging adds value to the ABCD2 score by identifying patients at a higher risk within a given ABCD2 score category. Because the ABCD2 score meaningfully stratifies risk within both tissue-positive and tissue-negative groups, it indicates that the score does more than simply separate "real TIAIs" from TIA mimickers. These findings add to the growing body of literature suggesting that early brain imaging (particularly DWI) enhances prediction of early stroke risk in patients with TIA.

In order to implement the author's findings into clinical practice, routine imaging in TIA evaluation protocols would be necessary. This would best be achieved with the use of MRI, rather than CT. Based on the author's results that patients with tissue-positive imaging after TIA had 7.5% more risk of having a stroke within the following week, one would need to image 14 (95% confidence interval 11–17.1) patients to identify one additional patient at high risk of early stroke. When extended out to assess the risk of stroke within 90 days, this number decreases to 11 (95% confidence interval 8.4–13.1). The authors appropriately conclude that the information provided by acute imaging is clinically relevant and should influence management and triage decisions.

The results of the study are valid, though there are some inevitable limitations. The data, pooled from 12 studies, were collected over 11 years from various medical centers with assessments by clinicians with different degrees of cerebrovascular experience and using different imaging techniques. This variation in study methods threatens validity to an extent, but also reflects the reality of clinical practice more accurately. Mixing results from CT scan and MRI appears most problematic, not only because of the higher sensitivity of MRI but also because DWI can demonstrate acute lesions while this is impossible with CT scans. Still, the overall rates of stroke at 90 days were similar in this study to those found in a
prospective study that used only MRI (current study had 2.2% vs 4.3% for tissue-negative and 12% vs 10.8% for tissue-positive).

Overall, these findings provide further support for the evolving concept of a tissue-based rather than the traditional time-based definition of TIA. The results make a compelling argument for the use of prompt brain imaging (specifically MRI with DWI sequences) to optimize the triage of patients with transient neurologic symptoms ascribed to focal cerebral ischemia. One specific interpretation of the data, when applying it to an emergency room situation, might be that patients with low risk ABCD2 scores (<3) with negative DWI could be discharged, while those with positive DWI should be admitted, despite the low ABCD2 score, given the substantial increased risk of stroke within the next 7 days.

Within the past few decades there have been tremendous advances in the diagnosis and treatment of cerebrovascular disorders. The results of this study support that our definitions and scoring systems should be correspondingly modified to maximize clinician decision-making with the aim of positively impacting on patient outcomes.

AUTHOR CONTRIBUTIONS
Dr. Fugate: drafting and revising the manuscript, interpretation of data. Dr. Rabinstein: revising the manuscript, interpretation of data, study supervision.

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Mystery Case

Interesting teaching cases submitted to the Resident & Fellow Section are chosen by the Resident & Fellow 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: 
Eyelid myoclonia with absences in an adult patient

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Figure 1 Eyelid myoclonia without absence

With levetiracetam: posterior-predominant spiky alpha frequency activity that rapidly spreads to the frontal regions coinciding with eyelid myoclonia.

A 28-year-old man presented to the epilepsy monitoring unit (EMU) with frequent "eye fluttering" episodes since he was 3 years old (video on the Neurology® Website at www.neurology.org). He was diagnosed with epilepsy as a teenager after he developed generalized convulsions at age 12. His convulsions were well-controlled with antiepileptic drug therapy. His neurologic examination was normal.

His EMU study revealed brief episodes of eyelid myoclonia (video) coinciding with a paroxysmal "spiky" posterior alpha activity, which rapidly spread to the frontal regions while he was on levetiracetam (figure 1). These episodes were more prominent in light compared to dark and were often triggered by eye closure. Interictally, the posterior dominant rhythm appeared sharply contoured. Discontinuation of levetiracetam for 3 days resulted in 2 to 3 Hz generalized polyspike and wave activity associated with some of the episodes of eyelid myoclonia, within seconds of eyelid closure (figure 2). Additionally, in sleep there were fragmentary bursts of anteriorly predominant 3 Hz abortive spike and wave discharges. Prior records indicated a photoparoxysmal EEG response.

The patient’s clinical and electrographic picture is consistent with eyelid myoclonia with absences (EMA), also known as Jeavons syndrome.

EMA is an underrecognized syndrome of unknown etiology defined by the triad of childhood onset, photosensitivity, and eyelid myoclonia with or without absence seizures.1,2 Patients often develop generalized tonic-clonic seizures in adolescence.1,3 The photosensitivity component may decrease as the patients get older.1,4 Classic EEG features include a sharply contoured or spiky alpha frequency activity that rapidly spreads to the frontal regions with sustained eye closure. Eyelid myoclonia often coincides as well with occipital epileptic discharges or occipital polyspike and wave discharges, with or without generalized polyspike and wave discharges.3 The overall prognosis of this syndrome is often good as the generalized tonic-clonic and absence

Supplemental data at www.neurology.org

From the Department of Neurology, Baylor College of Medicine, Houston, TX.
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.
seizures become controlled with antiepileptic drug therapy. Despite the sensitivity of the absences to antiepileptic drugs, the eyelid myoclonia often persists, as seen in our patient. A small proportion of patients may continue to have uncontrolled generalized convulsions. Valproic acid, lamotrigine, and levetiracetam are good treatment options, whereas sodium channel agents such as carbamazepine may exacerbate the seizures. Our patient initially responded to valproic acid, but he developed a reaction concerning for Stevens-Johnson syndrome. With levetiracetam treatment, his generalized tonic-clonic and absence seizures resolved.

Most adult patients with EMA are diagnosed in childhood, but making the diagnosis in adults for the first time may be challenging. Neurology residents and fellows should be aware of the characteristic clinical and electrographic features of this underrecognized syndrome.

AUTHOR CONTRIBUTIONS
Dr. Hannawi analyzed and interpreted the data, drafted and revised the manuscript. Dr. Santrute analyzed and interpreted the data. Dr. Maheshwar analyzed and interpreted the data, reviewed and revised the manuscript.

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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 answers that we received came through social media from individuals rather than groups.

Most of the respondents (66%) correctly indicated Jeansons syndrome as the most likely diagnosis. The other preferred response was absence epilepsy. The most complete answer came from Dr. Elippe Borlot (Clinical Fellow, Toronto Western Hospital and University of Toronto, Canada). In his response, he pointed out that the key element for this Mystery Case is the fact that these reflex seizures are induced by eye closure and that the epileptiform abnormalities disappear with eye opening. The eyelid myoclonia in this patient is characteristic. Jeansons syndrome can be misdiagnosed as childhood or juvenile absence epilepsy, other forms of genetic or idiopathic generalized epilepsies, or even facial tics.

This Mystery Case illustrates a classic epilepsy syndrome, usually refractory to treatment, which persists throughout life.

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Mystery Case:
A young boy with myoclonic jerks

SECTION 1
A 16-year-old right-handed boy presented for consultation for recent development of seizures. He is the product of a normal pregnancy and delivery without a history of developmental delay, head trauma, or family history of epilepsy. A year and a half prior to our consultation, the patient noted that his hand would suddenly jerk across the page while writing in his morning classes. Stress would exacerbate the jerks. Six months later, after staying up late the previous night, the patient awoke early and began to play on the computer when both of his hands suddenly jerked multiple times. He then fell over and began seizing. His mother witnessed tonic contraction of his body followed by clonic activity. He was brought by ambulance to the nearest hospital where a CT head was reported normal.

The patient had a routine EEG at an outside institution and was diagnosed with juvenile myoclonic epilepsy (JME). Valproic acid was started; however, despite increasing dosages, his jerks persisted. The patient then developed episodes of seeing blue, red, and white lights in his right eye followed by right-sided headaches. He underwent video EEG monitoring and was told that these visual symptoms were seizures. His valproic acid was increased and levetiracetam was added. Despite these medications, his jerks and visual seizures continued. Upon consultation with other neurologists, who all believed that the patient had JME, topiramate was added without clinical improvement. Immediately prior to the consultation at this institution, the patient had another generalized tonic-clonic seizure while attending an economics conference. Despite having been a straight-A high school student, he began to have increased difficulty with cognition and his mother pulled him out of school.

Physical examination revealed a well-appearing boy. Mental status was notable for difficulty with serial 7s and spelling backwards. Cranial nerve examination was normal. Frequent twitching were noted around his mouth and eyes. Strength was full and sensation was intact to all modalities. Coordination, reflexes, and gait were all normal.

Questions for consideration:
1. What is the differential diagnosis? Is it possible that the patient has something other than JME?
2. What is the next step in management for this patient? What testing would you order?

Video EEG showed moderate generalized slowing with frequent right-greater-than-left posterior spikes and very frequent bursts of diffuse 5–8 Hz polyspikes and wave activity (figure). The patient displayed brief, nearly imperceptible pauses and difficulty with comprehension during the generalized polyspikes. In addition, he had occasional myoclonic jerks preceded by a polyspike. Complaints of "having a thing in my eye" corresponded to a 20-second right occipital seizure. Valproic acid level was therapeutic at 89 µg/mL. MRI brain showed some occipital atrophy.

Questions for consideration:
1. What are the typical EEG findings of JME? What do the patient’s EEG findings suggest?
2. What additional tests would you order based on his clinical story and these EEG findings?
SECTION 3

Typical interictal EEG findings in JME consist of an irregular mixture of 3- to 6-Hz spikes, polyspikes, or slow waves with fragmentation on top of a normal background with ical generalized bursts of multiple spikes during myoclonic jerks. The patient’s EEG showed moderate generalized slowing of the background in addition to spikes over the posterior regions (figure). The presence of EEG background slowing can help distinguish between PME and JME since it is present in PME and not in JME. However, certain PMEs such as Unverricht-Lundborg and Lafora body disease can often present with a normal EEG background early in the disease course, thus leading to an initial misdiagnosis of JME. A way to differentiate Lafora disease from the other PMEs is the presence of occipital seizures with visual phenomena and the presence of spikes over the posterior regions on an EEG. Thus, genetic testing was sent and skin biopsy was performed to evaluate for Lafora bodies. The skin biopsy was negative for Lafora bodies. However, genetic testing revealed homozygous deletions in the EPM2A gene.

**Question for consideration:**

1. What treatments are available for Lafora body disease?
SECTION 4
Antiepileptic drugs (AEDs) remain the standard therapeu-
tic treatment for Lafora body disease. The first-line
agent remains valproic acid given its usual effectiv-
ess against myoclonus and generalized tonic-clonic
seizures. AEDs such as levetiracetam, zonisamide, lamotri
gine, topiramate, and benzodiazepines may also be help-
ful. One should avoid phenytoin, carbamazepine, and gabapent
in given their ability to potentially worsen myoclo-


dus.4 The ketogenic diet has been tested in a small pilot
study of Lafora body patients but has not been shown to
slow progression.9 Since Lafora body disease is known to
be resistant and progressive despite aggressive AED
management, treatment remains largely palliative.

Since the initial consultation, the patient’s seizure
frequency worsened and his cognition declined. He
was unable to graduate from high school despite
home tutoring. High-dose lorzepam monotherapy
has proven to be the most effective with the fewest
side effects. He is currently wheelchair-bound and has
frequent myoclonic and generalized seizures.

Interestingly, the patient’s myoclonus was observed
to be more symptomatic during the day than at night-
time. His mother notes that when she covers his eyes
she can often lessen the myoclonic jerks and abort a
generalized convulsion. She has taken to patching
his left eye in order to help stop the jerking and
seizures. He was evaluated at our institution by
neuro-ophthalmology and given 3 pairs of FL-41
glasses to try at home: dark pink, light yellow, and
regular dark. His mother reported that his myoclonus
was somewhat better with the regular dark glasses but
remarkably improved with the dark pink glasses.

DISCUSSION Lafora body disease is one form of
PME. PMEs are a group of disorders characterized
by focal and generalized seizures, myoclonus, and
progressive neurologic dysfunction, usually with

cognitive deterioration and ataxia.6 The other com-
mon PMEs include Unverricht-Lundborg disease
(Baltic myoclonus), MERRF, neuronal ceroid lipofus-
cinosis, sialidoses, and dentatorubral-pallidoluysian
atrophy.

Lafora disease has a typical onset between 12 and
17 years of age. Before onset, children are typically of
normal intelligence and physical development.7 This
can make initial diagnosis difficult to distinguish from
typical idiopathic generalized epilepsy. Seizure types
can include myoclonus, occipital seizures with tran-
sient blindness or visual hallucinations, atypical
absences, and atonic and complex partial seizures.
Dysarthria and ataxia can also present early on in
the disease. Cognitive decline accelerates and demen-
tia occurs later in the disease. As the frequency and
severity of seizures worsen, status epilepticus can
occur. Many individuals die within a decade from
diagnosis, typically from status epilepticus or aspira-
tion pneumonia.4

Early on, EEGs show a well-organized background
with multiple spike and wave activity and photosensi-
tivity. However, as the disease progresses, the EEG
will show an abnormally slow background with
loss of sleep features. Bursts of multifocal spike and
wave discharges are seen with an occipital predomi-
nance. The spike and wave pattern changes from a
frequency of 3Hz to 6–12 Hz.4

Lafora body disease is an autosomal recessive dis-
order characterized by mutations in the EPM2A gene
encoding laforin phosphatase or the EPM2B gene
encoding maln ubiquitin E3 ligase.5 The malfunction
of these genes results in the formation of abnormal
glycogen that accumulates in the brain called Lafora
bodies. Thus, Lafora bodies are polyglucan inclusion
bodies within neurons that stain positive with periodic
acid–Schiff. Lafora bodies can also be found in liver,
muscle, sweat glands, and apocrine myoepithelial cells,
though it is asymptomatic in these organs. A skin
biopsy of the axilla can aid in diagnosis; however, it
does not have perfect sensitivity.7 Genetic testing shows
mutations in the EPM2A or EPM2B genes.

Treatment includes AEDs such as valproic acid,
benzodiazepines, zonisamide, and levetiracetam. Again,
one should avoid myoclonus-aggravating drugs such as
phenytoin, carbamazepine, and gabapentin. In this
patient, it was interesting to note the improvement in
myoclonus with patching of one eye and the use of pink
lenses. The use of colored glasses may provide some
relief for those with photosensitive epilepsy, although
this is controversial.8 Given the natural history of
the disease, it is expected that the patient’s seizure
frequency and severity will continue to worsen despite
treatment. Lafora disease is progressive and fatal usually
within 10 years after clinical onset. Genetic counseling
as well as social and psychological support should be
offered to families.

AUTHOR CONTRIBUTIONS
Camelia Mulesh: drafting/revising the manuscript, analysis or interpreta-
tion of data, accepts responsibility for conduct of research and final
approval, acquisition of data. Lara Marcuse: drafting/revising the manu-
script, analysis or interpretation of data, accepts responsibility for conduct
of research and final approval, study supervision. Madeline Fields: draft-
ing/revising the manuscript, study concept or design, analysis or interpre-
tation of data, accepts responsibility for conduct of research and final
approval, acquisition of data, study supervision.

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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 answers that we received came through social media, from individuals rather than groups. Most of the respondents (42%) correctly indicated Lafora disease as the most likely diagnosis. Other considerations included JME (33%) and the idiopathic occipital epilepsy of Gastaut (10%). The key element was the identification of a slow posterior dominant rhythm in the EEG recording. While this can occur in any chronic epileptic encephalopathy, it is commonly seen in the progressive disorders, like the PMEs.

The most complete answer came from Dr. Alexis Dallara (Child Neurology Fellow, New York-Presbyterian University Hospital of Columbia, New York). In her response, she pointed out that Lafora disease “presents with seizures, usually myoclonic, clonic or focal, and often has predominant occipital paroxysms on the EEG.” In her differential diagnosis, Dr. Dallara considered the idiopathic occipital epilepsy of Gastaut and the idiopathic photosensitive occipital epilepsy. She correctly indicated that epilepsy with grand mal seizures on awakening, as well as JME, are less likely, due to the presence of occipital paroxysms. This Mystery Case illustrates a rare etiology for epilepsy, although one of the most common PMEs. Lafora disease is a fatal autosomal recessive genetic disorder characterized by the presence of cytoplasmic inclusion bodies, known as Lafora bodies, within neurons, and was named after Gonzalo Rodriguez Lafora (1886–1971), a Spanish neuropathologist.

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Resident & Fellow Section: Call for Authors Initiative

Residents & Fellows can visit the Call for Authors page and sign up to ‘check out’ a topic: Neurology.org/site/feature/callforauthor.xhtml. The R&F editorial team has listed topics under the following categories: Emerging subspecialties, Book and Media reviews, Child Neurology, Journal Club, and Opinion and Special Articles. Interested submitters can ‘check out’ a topic and submit a manuscript within six weeks of commitment.
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.
Opinion & Special Articles:
Neurology training
To pursue or not to pursue a fellowship

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The present-day burgeoning of new medical information, interventions, and procedures, as well as the emphasis on quality improvement, has fostered a greater need for specialization in medicine. More residents than ever before are pursuing a fellowship, and neurology residents are no exception. Approximately 86% of neurology residents matriculate into a fellowship, up nearly 10% from a decade ago. Although not all fellowships are accredited by the Accreditation Council for Graduate Medical Education, and applying for neurology fellowships is hardly a standardized process, the statistic suggests that residents value additional training (table). However, fellowships are not for everyone, and there remain compelling reasons for some residents to forgo fellowship in favor of a clinical position directly out of residency.

ADVANTAGES Many factors weigh in on an individual's decision to pursue fellowship directly after residency. During this unique period of time, general neurology preparation peaks in preparation for the board examination, and there is strong motivation to pursue further training, as evidenced by increasing rates of fellowship matriculation. Although limited data exist among neurology residents and fellows, a survey of postgraduate neurosurgical residents found that among the most important factors contributing to this decision is with an additional 1 or 2 years of training, fellows are able to attain greater academic prestige and gain valuable experience in a particular subspecialization of personal interest. Fellowship allows residents to focus on a high volume of patients with a relatively narrow spectrum of neurologic pathology.

The fellow's specific expertise, experience, and level of responsibility increase with additional specialty training. They are able to essentially function as an attending but with the benefit of having an experienced specialized physician as a safety net. In addition, procedure-heavy fellowships, including electrophysiology and endovascular surgical neuroradiology, provide much-needed procedural skill instruction, permitting fellows to gain a comfort level and fulfill requirements for board certification otherwise unattainable with residency alone. The majority of neurosurgical residents feel they have inadequate exposure to endovascular surgical neuroradiology, and it is not difficult to imagine that neurology residents have even less exposure, if any. Even for those residents pursuing inpatient general neurology or a neurohospitalist position, in which they would be required to manage a wide spectrum of neurologic illness from stroke to rapidly progressive dementia, a fellowship may strengthen areas in which their residency training was deficient. A common area of deficiency with neurology residency training lies in teaching the "business of neurology" and at least 70% of residents reported inadequate training in this area in the 2012 neurology resident survey. Postgraduate education provides one avenue to gain familiarity with the practical aspects of medicine including optimizing reimbursement with effective coding and billing strategies.

Most neurology practice opportunities in both private and academic settings prefer fellowship-trained physicians. However, added experience is only a part of the competitive advantage attained through this additional training. During fellowship, fellows can explore their research interests and increase their publications to further strengthen their job applications. The benefit of mentorship in research productivity has been extensively studied in academic medicine. A case-controlled study comparing fellows paired with a mentor and fellows without a formal mentor-based fellowship program showed that the opportunity to cultivate a strong relationship with a distinguished mentor in a mutual area of interest was associated with a greater number of publications and academic success. This relationship is invaluable when later seeking an academic position, where such subspecialty circles are often small and personal recommendations are heavily weighed. Fellowship can also provide increased time for meetings and research presentations, fostering networking in an effort to facilitate the next career move.

Approximately half of all residents will leave their residency training institution to pursue fellowship.

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Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
allowing them the advantage of networking at another facility while maintaining their connections and contacts from residency. It also provides the opportunity to gain new perspectives and exposure to different treatment approaches. However, those with established roots in their fellowship institution may be reluctant to leave a comforting training environment where the system is familiar and transition to an attending position is even easier.

If residents are undecided about their future specialty, fellowship can yield insight into a prospective specialty without necessarily committing to that field. Many fellowship programs also provide additional exposure to the academic setting, including the opportunity to take on a larger role in undergraduate and graduate neurology education, giving undecided fellows insight into their future should they choose to pursue work in an academic environment. For residents with US federal student loans, an extra year of fellowship is an extra year that undergraduate, graduate, and medical student loans can be deferred, albeit at the expense of an attending salary. Ultimately, fellowship provides extra time to make important decisions about the residents’ future, including what type of lifestyle they want to pursue and where they wish to settle.

DISADVANTAGES As the vast majority of residents favor specialty training, it is not surprising that there are few disadvantages to pursuing fellowship, although there are valid reasons to not extend training. Many residents, after completing residency at a busy academic center, are already well-trained, confident, and sufficiently experienced to function as general neurologists. In addition, some neurology programs offer focused elective time, particularly in EMG training, so residents can not only become proficient in performing and interpreting EMGs, but also meet requirements for board eligibility during residency without having to complete a separate year of fellowship. In these situations, a year of real-world experience may hold greater educational value than a year of fellowship training.

The ever-changing climate of reimbursement, which has negatively affected electrodagnostic medicine, among other subspecialties, is another reason to be cautious of specialization. Those residents pursuing fellowship primarily for lucrative and billable procedures must
realize the landscape of neurology is undergoing a transition, and it may not be as financially advantageous to pursue specialty fields for their monetary benefit alone. This is exemplified by the recent negative interventional trials, which affected reimbursement, leading some to consider the indefinite suspension of all neurointerventional training programs. Those who practice general neurology, perhaps even after completing a fellowship, will always be in demand, as compared to those who subspecialize, particularly if that skill will no longer be reimbursed.

Often, older residents, or those who may have transitioned to neurology after initially pursuing a different field, may elect not to spend another year in training with a suboptimal salary in favor of settling down in an attending position.

Nearly half of all neurology residents and fellows graduated from medical school outside of the United States. Because some fellowship programs do not sponsor an H1 visa, the benefits of pursuing a private practice or attending position in a desirable location may be more attractive than a year of fellowship in a less than desirable location or field of interest. Another disadvantage in the increased number of residents pursuing fellowship affects not the residents but rather the patients. The need for general neurologists continues to grow; however, greater fellowship training may lead to a relatively smaller proportion of general neurologists, and subsequently higher wait times for patients.

**DISCUSSION** Fellowship after neurology residency is becoming increasingly popular. It offers a number of advantages, including additional specialty experience, a competitive resume, and academic prestige. However, some elect to forgo fellowship out of necessity and a desire to gain practical experience in a private practice or academic setting. With the increasing number of fellowship-trained neurologists, the need for well-trained general neurologists who see the vast spectrum of neurologic illness, from headaches to nonspecific gait disorders, should be emphasized. The increasing trend in pursuing fellowship training should be equally encouraged as it represents a genuine attempt, motivated by scientific interest and curiosity, toward the mastery of one of the many pinnacles of subspecialty neurologic training. However, we must take care not to become that specialist who knows more and more about less and less, until finally knowing everything there is to know about nothing at all.

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Opinion & Special Articles:
A guide from fellowship to faculty
Nietzsche and the academic neurologist

ABSTRACT
The role of the physician scientist in biomedical research is increasingly threatened. Despite a clear role in clinical advances in translational medicine, the percentage of physicians engaged in research has steadily declined. Several programmatic efforts have been initiated to address this problem by providing time and financial resources to the motivated resident or fellow. However, this decline in physician scientists is due not only to a lack of time and resources but also a reflection of the uncertain path in moving from residency or postdoctoral training toward junior faculty. This article is a practical guide to the milestones and barriers to successful faculty achievement after residency or fellowship training. Neurology 2012;79:e116-e119

Physician scientists have a critical role in the translation of biomedical discoveries to clinical treatments. With training and perspective in both basic science and clinical aspects of medicine, physician scientists are in a position to identify potential clinical applications in basic mechanistic discoveries, and play an important role in the design and conduct of clinical trials for the treatments that arise from these discoveries.1,2 Within neuroscience research, physician scientists have identified new routes to stimulate plasticity in the brain,3 developed a genetic characterization of progenitor cells in the adult brain,4,5 and new cell-based therapies from these studies.6

Notwithstanding these advances, the status of the physician scientist within the biomedical enterprise is threatened. The percentage of physicians engaged in research has declined steadily from a peak in 1985 to a level of 1.8% in 2003.7 There are 25% fewer academic physicians than 10 years ago.8 This decline in the number of physician scientists occurred though the NIH budget went through a doubling phase during this period. Despite these statistics, the number of medical students expressing an interest in research, the number of MD trainees interested in research, and the number of MD/PhDs have grown since 1999.7 The continued interest in research by early medical trainees presents opportunities for a change in physician scientist training that might produce more success in the pathways that move forward in this field.8,9

THE CRITICAL PERIOD Simply conducting research during a training period by itself has not translated into successful physician scientists. In recent data from NIDA, trainees with 1999 and 2000 career development awards tended to stay in academia after the award and publish, but few received grants (19%–22%).10 This junior faculty interval after the career development award is a critical period. If physician-investigators are able to either renew their first RO1 grant or obtain a second RO1 grant, they are likely to remain in the investigative career track.11 Practical advice is needed for physician scientists as MD NIH RO1 applicants are considerably less successful than PhD or MD/PhDs in obtaining independent grant funding.12

THE PREREQUISITES: CHOOSING A RESEARCH AREA AND LOCATION, AND PROVIDING VALUE TO THE UNIVERSITY/HOSPITAL The most important characteristic in choosing a research area is to identify the topic that brings forth the most passion. This concept has evolved into a bit of an aphorism: one must be passionate about one’s research. This is no more true than for the physician scientist because of

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the huge number of roadblocks put into his or her path. The financial roadblocks are the most obvious. But other roadblocks are no less daunting. Physician researchers are more likely than other scientists to trip the oversight of possibly every regulatory bureaucracy in the academic institution: the animal research committee, the human studies board (institutional review board), the Environmental Health and Safety review board (for laboratory safety), the Biosafety Committee (for transgenics and viral gene delivery), the embryonic stem cell oversight committee, the radiation safety committee, and, lately, the financial conflict of interest committee. These agencies exist to safeguard the institution, and are beholden to it and not the investigator. It is likely that the research career of any scientist is spent in countless hours satisfying an evolving series of queries from one or more regulatory agency. If the creative enterprise of scientific study is what lured many physician scientists toward research, it is the steady drip-drip-drip of regulatory compliance that may drive them out. One needs to be fired up over a research project to be able to surmount the energy-sapping process of maintaining approval from all regulatory groups that seek to control it. The physician scientist has a unique understanding of the relevancy of his or her studies for clinical translation and this can also lead to a passion that may overcome the myriad regulatory hurdles.

Postgraduate researchers who enter the faculty track must also choose a research location. Despite the promise of Web interactions and social networking, the most successful collaborative research occurs on a local scale, often within the same building. Indeed, buildings with the most successful collaborations produce articles with the greatest impact factor. It is a lot easier to move to an institution with the appropriate facilities and collaborators at an early stage of one’s career. Mentoring is another key factor that needs to be present in the local environment and is discussed below.

An academic physician is evaluated by his or her employer based on the value he or she provides to the department and the university/hospital. The choice of research, clinical work, and teaching must provide value for the institution (money, prestige) or be valued by the institution. As a career evolves, faculty often maximize their value to an institution through their indirect costs from grants—providing far more money than clinical reimbursement. This allows a buying out of extended clinical commitments for more direct research time. At an early career stage this is usually not possible. An academic physician should choose a research field that will provide a clinical niche that takes them out of the burden of providing extensive general medical care. In neurology, programs within the wider department provide natural niches: including stroke, movement disorders, epilepsy, and neurorehabilitation.

Protected time that is dedicated for research is the absolutely essential element in establishing a productive research program. Consequently, the amount of protected time is a key negotiating item in a starting position. Experience indicates that the amount of protected time needs to be >70%. This number is reflected in most training grants. The burden of support for junior faculty protected time comes from the institution—it is their investment in the young investigator and a barometer of their interest. As noted in an excellent review, there are warning signs for a lack of protected time at an institution: frequent moving of junior faculty or high turnover; clinical coverage that appears very fluid and may serve to cover senior faculty clinical or teaching schedules; and the placement of junior faculty in administrative positions as course directors, heads of training programs, or clinics.

THE DOLLARS The current financial situation is characterized by aging grants, competitive and uncertain funds, and evolving ideas for national research resource allocations. These factors mean that aiming for the right grant is essential. Aiming for the right grant means choosing the right research project. There are several simple rules for choosing the right project. First, avoid a research project that is interesting but unfundable. While this sounds like common sense, many junior faculty still fail to heed warnings from colleagues about this. Second, the research project must be interesting to the researcher. A mentor or forceful colleague may present a compelling set of ideas, but a young investigator must be able to say no if the project is not interesting (see passion, above). Third, the research project must pose a new question: a search of the NIH grant database and (as always) a thorough reading of the literature determines novelty. Fourth, the research project must suggest a meaty set of studies. The successful project will be a multyear endeavor that sustains an inquiry with greater detail and focus over time. A proposal in which only studies for the first year are easily designed is bound for failure. Fifth, the project must be practical for the local scientific environment—people who have expertise in the methods and instruments, cores or clinical resources that will support the proposed studies should be in proximity.

The final 2 rules in choosing a research project are less dogmas than mantras: discuss, discuss, discuss and (with Thoreau) simplify, simplify, simplify. A research idea must be discussed thoroughly with colleagues and mentors. It is useful to bounce the Specific Aims page off of senior colleagues, as the whole grant may demand too much time for thorough review. Simplify the grant in formulating the actual
research plan. The grant should be written with direct and well-conceived studies, which have logical and simple relationships to the hypotheses/aims, and easy-to-understand limitations and work-grounds.

Once the right research project is identified, choosing the right grant can be broken down into 2 time epochs: very early stage (1 to 1 ½ years after residency/postdoctoral fellowship) and early stage (after this period but before major grant support). Very early stage is the period before the data and projects are well-developed. This stage is often premature for assembling a full package of studies and career development that are required in a K award. With only one resubmission it is inadvisable to make a good research project by submitting too hastily. At this very early stage the young investigator can focus on foundation, industry, and institutional grants, such as those from the American Heart Association, American Federation of Aging Research, pharmaceutical companies, and disease-specific foundations. The NIH F32 grant (postdoctoral grant) is also an option but places the investigator fully under a mentor. Grant search engines may help in identifying some of these perhaps more far-flung but still important funding opportunities: Community of Science, Grants.gov, Grantsnet, and the Illinois Researcher Information Service. An important element in this process is that, though a grant may not be funded, a good grant is reviewed by senior scientists who are associated with all of these funding agencies. They will remember the name of the investigator and the quality of the ideas and science. This is a bit of networking that will help in future manuscript and grant submissions. This networking aspect to the junior faculty transition extends beyond grant applications. Data abstracts at meetings, talks, and in symposia all help with establishing a link with more senior scientists to one’s work.

Early stage grant applications should include mentored career development awards: K08 and K23. These are well-discussed on the NIH Web site and in FAQ pages. These grants provide the first chance to be principal investigator on a grant, although associated with a mentor. Successful K applications require a strong institutional commitment, including a Chair’s letter, training plan, and concrete commitment of space, and with recent competition in this grant category, usually a recent primary research publication is necessary.

THE CLOCK The 7-year clock is in effect at most institutions: the time from initial appointment as a junior faculty member to a final tenure disposition. The most important element in successfully negotiating this time period is to establish a milestone-driven timetable. The time from completion of residency to tenure seems long. This means there is a possible loss of sense of time and of the process for hitting deadlines. An excellent example of a detailed timetable can be found in the HHMI resources Web section. Be aware of key milestones toward promotion. The timeline from the department’s perspective is that in years 2 to 3 the department will create a dossier of research, teaching, and clinical output. By the end of the third year, tenured faculty vote or participate in some sort of mid-year assessment. In years 5 and 6, comments are solicited from internal and external experts on the academic output and from former students or trainees on teaching and mentorship. In year 6, the department votes on the tenure decision and this is then sent to the university committee on academic promotions. In addition to establishing a timetable, it is important to minimize clinical commitments, maximize protected time, and establish strong mentorship. It is always tempting to diffuse one’s time to help out a colleague by providing coverage for a busy service, but a junior faculty member has to say no if he or she wants to succeed. Mentoring includes both formal mentoring interactions, often set in place by the department, and informal mentoring from respected colleagues. Useful indicators for a good mentor are the depth of past experience in mentoring trainees and the presence of independent research funding, particularly peer-reviewed grant support.

THE PEOPLE In planning a laboratory or negotiating for resources, it is important to focus on people and not just on space and equipment. The people in the laboratory are going to get things done and successfully run the infrastructure. In a basic science laboratory, it is important to strongly consider an initial hire to be a medium to senior level technician. This person will be able to perform the experiments without labor-intensive oversight, and can assist in training new people. Besides this technical hire, it is important to find trainees. A junior faculty member should take some of the (hopefully small) mandatory teaching commitments and volunteer for teaching assignments that will produce exposure to trainees. Avoid the animal research committee and human studies institutional review board at early career stages and focus on admissions committees, conference or seminar organizing committees, and teaching positions that expose a faculty member to potential trainees before they have chosen a laboratory or clinical research setting.

PAPERS: HIT SINGLES In planning research publications, focus on research quality and hit the academic goals that you have established, but aim for solid and reachable publications. Do not try to hit an initial home run, and risk the time and personal cost in whiffing
several times. There is nothing more paralyzing for a grant application than to have the key supportive data tied up in a manuscript that is taking the slow scenic tour of high-impact journal reviews. There are 2 main reasons for hitting the single when it comes to publishing. If put together correctly, this type of paper is a unitary output that can advance the field and one’s career in a measurable, concrete fashion. It is also less prone to hyperbolic peer review. Saul Bellow wrote: “I discovered that rejections are not altogether a bad thing. They teach a writer to rely on his own judgment and to say in his heart of hearts, ‘To hell with you.’” Publishing solid and regular manuscripts gives the young investigator the strength of character when the inevitable bitter reviews come curving toward the plate.

A WORD ABOUT COLLABORATION “The Main Thing is to Keep The Main Thing the Main Thing.” The junior faculty member has identified his or her Main Thing. He or she does not want others to drag them into their Main Thing. It is best to avoid distributed collaborations, in the beginning of one’s career, in which research questions are shared at the primary stage and papers and grants are evenly split; and to collaborate as needed to bring in new methods, instruments, or approaches. In these cases the research idea is the junior faculty’s, and help with the methods or implementation comes from a collaborator. This process is easier to trace by committees on academic promotion. After tenure is established, or substantial peer-reviewed funding and publications are produced, collaborations that are more equal or far-flung provide interesting research directions and creative stimulation.

THE MAJOR BARRIER: NIETZSCHE AND THE ACADEMIC NEUROLOGIST Most investigators run into barriers. Usually one major barrier presents itself. The key method is not in the laboratory, the most important new piece of equipment is not available, the coolest technique for studying a phenomenon is not within easy reach. These key barriers are often in the “break-away” process—that one thing that might allow one’s research to break away from the others and establish a really rigorous, complete or novel approach. This is the gut-check moment for young investigators—Will you bring this in? Will you innovate? Young investigators should work to identify the limits that are preventing their research program from truly transformative experiments, then seek opportunities to capture these approaches. Collaborators may provide the solutions, such as applying for a small grant to fund these studies, or traveling to observe the technique and bring it back. Successful scientists fill in their missing link. In fact, successful scientists at all levels are often defined by scientific publications that result from the extra effort to surmount a weakness. That which does not kill us makes us stronger.

DISCLOSURE
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REFERENCES
Pearls & Oy-sters

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

PEARLS

- Voltage-gated potassium channel (VGKC) antibody–associated encephalitis is a well-known form of limbic encephalitis characterized by acute to subacute onset of confusion and cognitive impairment, mediodentate sclerosis, and psychiatric disturbances.
- Among other causes of rapidly progressive dementia, this condition is responsive to immunotherapy, and therefore correct and early diagnosis is crucial.
- Sporadic Creutzfeldt-Jakob disease (sCJD) typically presents with rapidly progressive dementia associated with a mixture of cerebellar, extrapyramidal, visual, behavioral, or psychiatric symptoms.

OY-STERs

- VGKC antibody–associated encephalitis may be confused with sCJD due to overlapping of clinical, neuroradiologic, and biochemical features. A careful and complete medical evaluation is imperative in order to prevent potential misdiagnosis of a reversible condition for a terminal one.

CASE REPORT

A 65-year-old woman was admitted after a 4-month history of rapidly progressive cognitive impairment. Her medical history was unremarkable without history of cigarette smoking, alcohol abuse, or neurologic or psychiatric illness. She was able to perform all activities of daily living until 4 months prior to evaluation, when she developed unusual behavior and memory impairment. She also complained of malaise and fatigue. Two months prior to evaluation, she began to have difficulty with her daily activities, developed depression, and developed more severe behavioral and memory problems. She was seen by a psychiatrist and underwent a brain MRI, which did not demonstrate any abnormalities. By the time she presented for neurologic evaluation, she had developed confusion and was unable to take care of herself. Due to the rapid progression of symptoms, the patient was admitted for further investigation.

Neurologic examination demonstrated no cranial nerve or sensory deficits. There was no weakness present but the patient did have extensor plantar responses bilaterally. Mini-Mental State Examination score was 19/30 (temporal and spatial disorientation with verbal learning impairment) and extensive neuropsychological assessment confirmed impairment of language (verbal fluency and naming), memory, and selective attention. The patient was also found to have fluctuations of consciousness as well as hallucinations. EEG demonstrated a background pattern of 7–8 Hz and slow biphasic and triphasic waves with higher amplitude in frontal regions (figure A). A few days after admission, the patient developed facio-brachial tonic seizures and generalized tonic-clonic seizures. The severity and frequency of seizures, as well as the EEG abnormalities (figure B), improved after treatment with levetiracetam. Neuropsychological features, however, remained unchanged. Standard blood examinations were normal. Blood tests were also negative for lupus anticoagulant, antinuclear antibodies, antibodies to extractable nuclear antigens, antineutrophil cytoplasmic autoantibodies, anti-cardiolipin antibodies, and cryoglobulins. Serum neoplastic markers and angiotensin-converting enzyme were within normal range.

Fluid-attenuated inversion recovery (FLAIR), T2-weighted, and diffusion-weighted imaging (DWI) MRI revealed areas of hyperintense signal involving the right hippocampal cortex and left striatum (figure C–E). Comparison with the apparent diffusion coefficient (ADC) map revealed restricted diffusion in the left caudate and putamen (figure F). CSF cell count and total proteins were normal; isoelectric focusing showed oligoclonal bands in serum and CSF. Serum and CSF antibodies against Borrelia burgdorferi and Treponema pallidum and CSF culture for bacteria and fungi were negative. CSF and blood nPCR assays were negative for herpes simplex virus 1 and 2, cytomegalovirus, HIV, Epstein-Barr virus, human herpesvirus 6, varicella-zoster virus, parvovirus B19, measles virus, adenovirus, and enteroviruses.

CSF examination revealed a markedly increased total tau protein (>1,200 pg/mL) and a positive 14-3-3 protein test. The level of the latter was calculated from the Department of Neuroscience (F.C., J.M., M.T., F.V., S.V., E.G., P.B., P.N.), S. Agostino-Estense Hospital and University of Modena and Reggio Emilia, Modena; and IRCCS Institute of Neurological Sciences of Bologna and Department of Biomedical and Neurorontor Science (DIBINEM) (C.S., R.L., P.P.), University of Bologna, Italy.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the author, if any, are provided at the end of the article.
EEG recordings show diffuse slowing with slow biphasic and triphasic waves with higher amplitude on frontal regions (A). EEG recording after oral treatment with levetiracetam shows the resolution of these waves (B). Brain MRI at admission: axial T2-weighted and diffusion-weighted imaging sequences demonstrate hyperintense areas involving the left striatum (C, D, arrow). Coronal FLAIR with hyperintensity of the right hippocampal cortex (E, arrow). Apparent diffusion coefficient map reveals normal diffusion coefficient in right caudate (F, circle 2) and restricted diffusion in left caudate and putamen (F, circle 1).

Semi-quantitatively by Western blotting, as described. Densitometric value of the 14-3-3 band in the patient was 5-fold higher than that of the internal control sample (non-CJD subject who had trace levels of 14-3-3 protein) and comparable to that of a typical sCJD case with methionine homozygosity at codon 129 in the prion protein gene (PRNP) and pathologic prion protein type 1 (MM1 type) confirmed at autopsy. PRNP analysis revealed methionine/valine heterozygosity at the polymorphic codon 129. Total body CT imaging, esophagogastroduodenoscopy, colonoscopy, and gynecologic evaluation were normal.

IV immunoglobulin (0.4 mg/kg/d for 5 days) and steroids (methylprednisolone 1 g/d for 5 days) were administered, followed by a course of oral corticosteroids (50 mg/d oral prednisolone). Three weeks later, the patient’s clinical condition began to improve and brain MRI showed partial resolution of the FLAIR, T2, and DWI hyperintensities in the right hippocampal cortex and left striatum. One month later, serologic evaluation revealed VGKC/leucine-rich glioma-inactivated 1 (LG11) autoantibodies. Screening for other autoantibodies, including onconeural antibodies (Hu, Yo, Ri, CV2, amphiphysin, Ma2) and autoantibodies against neuronal surface antigens (AMPA, NMDA, CASPR2), was negative.

Three months after her initial presentation, a second cycle of IV immunoglobulin and steroids followed by oral corticosteroids was administered. The antiepileptic therapy was modified, with gradual introduction of lamotrigine (up to 200 mg/day) followed by discontinuation of levetiracetam. In the following months, the patient’s condition continued to improve. There was a disappearance of seizures and a progressive recovery of memory function, confirmed by neuropsychological testing.

A repeat CSF assay performed 2 weeks after the second immunomodulatory therapy cycle revealed normal level of both 14-3-3 and total tau proteins. Four months later, brain MRI showed a further reduction of the hyperintense signals in all affected areas. At the most recent visit, 1 year after her initial presentation, the patient has remained seizure-free for 8 months, was oriented, and showed improved memory.

**DISCUSSION** Due to the rapidly progressive onset and course of cognitive and behavioral impairment, VGKC antibody–associated encephalitis may present similarly to sCJD. sCJD, the most common human
prion disease, is a phenotypically heterogeneous disorder including at least 6 distinct subtypes, which are largely determined by genotype at the polymorphic codon 129 (encoding methionine or valine) in the PRNP and by the type (type 1 or type 2) of the abnormal prion protein accumulating in the brain.3

Due to the wide and often nonspecific clinical phenotype, the differential diagnosis between sCJD and other rapidly progressive dementias, including autoimmune encephalitis, mainly relies on neurophysiologic, imaging, and laboratory testing. Among them, EEG criteria have the lowest sensitivity and specificity, since the supportive diagnostic pattern (e.g., periodic 1–2 Hz triphasic sharp waves) develops in only about two-thirds of sCJD cases and can be seen in a variety of other diseases (e.g., toxic-metabolic conditions, dementia at the later stages, Hashimoto encephalopathy).4

CSF protein assays based on protein 14-3-3 or total tau detection have higher sensitivity and specificity than EEG recording, the latter ranging from 80% to 95% in most studies, but remain of moderate diagnostic accuracy, especially in cases that are associated with a low pretest probability of having sCJD.5

A relatively high sensitivity and specificity for sCJD have also been reported for brain MRI; around 80% of patients have been reported to have DWI or FLAIR abnormalities in cortex or deep grey matter structures (striatum and thalamus).6,7

Recently, Vitali et al.8 suggested that prevalence of DWI over FLAIR abnormalities, implying restricted diffusion, is one of the most important criteria for diagnosing sCJD, suggesting also that the presence of hypointense regions on ADC is a supportive feature of sCJD and may be helpful to distinguish mimicking diseases. Moreover, only sCJD cases had DWI subcortical hyperintensity correlating with ADC hypointensity in the same regions: this finding is highly specific for sCJD in the proper clinical context.8

Given the phenotypic heterogeneity of sCJD, a correlation between MRI lesion patterns and molecular subtypes has also been attempted.9 Although the cerebral cortex, basal ganglia, and thalamus showed a different pattern of involvement among sCJD subtypes, hippocampal signal alterations in both DWI and FLAIR were present in more than 30% of patients,9 including the MV1 subtype.9

In our case of rapidly progressive dementia, the brain MRI abnormalities, EEG findings, and elevation of CSF 14-3-3 and tau protein were initially compatible with a clinical diagnosis of probable sCJD. Only the clinical course and the positivity for anti-LGI1 antibodies led to the right diagnosis. The presence of faciobrachial tonic seizures that may be associated with VGKC antibody–associated encephalitis led us to the decision to treat with immunosuppressants even though the hypothesis of autoimmune encephalitis was not supported by the initial imaging and laboratory findings. Indeed, VGKC antibody–associated encephalitis is a significant diagnostic challenge to clinicians due to its rarity and substantial heterogeneity. Rapidly progressive cognitive decline, behavioral changes, depression, emotional lability, and seizures are the most frequent clinical presentation of the disease.4 Treatment for VGKC antibody–associated encephalitis involves immunosuppressive therapy consisting of plasma exchange or IV immunoglobulin followed by oral corticosteroids. A prior case series has shown that combination of these agents resulted in a decrease in the levels of serum VGKC antibodies and in a variable improvement of neuropsychological functioning,10 as in our case.

Clinical, radiologic, electrophysiologic, and laboratory findings in VGKC antibody–associated encephalitis may overlap with those of sCJD, leading to a difficult differential diagnosis. All individuals with rapidly progressive dementia should be assessed for the possibility of antibody-mediated encephalitis. This assessment should include early serum testing for antibodies against voltage-gated potassium channels. While awaiting final serologic results in patients with a rapidly progressive dementing illness, it may be reasonable to try an empiric course of immunomodulatory therapy.

AUTHOR CONTRIBUTIONS

Dr. Cavallieri: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript. Dr. Mandrioli: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, study supervision. Dr. Tondelli: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, study supervision. Dr. Vicenna: study concept and design, analysis and interpretation of data. Dr. Vallone: acquisition of data, analysis and interpretation of data, study supervision. Dr. Georgoulopoulou: acquisition of data, analysis and interpretation of data. Dr. Barbi: acquisition of data, analysis and interpretation of data. Prof. Liguori: acquisition of data, analysis and interpretation of data. Prof. Parchi: acquisition of data, analysis and interpretation of data, drafting of the manuscript, study supervision. Prof. Nichelli: study concept and design, study supervision.

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Pearls & Oy-sters: Trigeminal autonomic cephalalgias

The trigeminal autonomic cephalalgias (TACs) are a group of primary headaches that are characterized by unilateral pain, a relatively short duration of symptoms, and associated ipsilateral cranial autonomic symptoms, such as Horner syndrome, lacrimation, and nasal congestion. Incidence is rare when compared to other primary headache disorders but diagnosis (and, more importantly, treatment) can prove to be a challenge even when presented with a typical clinical presentation. The TACs are listed in the International Classification of Headache Disorders (ICHD-II) under their own section and include the following:

1. Cluster headache (CH)
2. Paroxysmal hemicrania (PH)
3. Short unilateral neuralgiform headache with conjunctival injection and tearing/cranial autonomic symptoms (SUNCT/SUNA)

See the table for a summary of treatment options.

Cluster Headache Pearl. All cluster headaches need to be treated with abortive, transitional, and preventive therapies.

Oy-ster. The average time it takes for a patient with CH to be correctly diagnosed is 6.6 years. The average number of physicians seen prior to correct diagnosis is 4, and the average number of incorrect diagnoses prior to a diagnosis of CH is also 4.2

CH has a very typical clinical presentation and for this reason, the aforementioned “oy-ster” is unacceptable as patients suffer needlessly. Cluster sufferers will attest to thoughts of suicide, as the pain is extremely severe, and CH is often dubbed a “suicide headache.”

CH comes in 2 epidemiologic forms. Episodic cluster, the more common form, is characterized by attacks that occur daily during a cluster period, the period of attacks generally lasting 1–3 months, and followed by months or even years of remission before recurring. In chronic cluster, attacks occur for more than 1 year without remission, or with remissions lasting less than 1 month.3

Attacks are strictly unilateral with associated ipsilateral cranial autonomic features, and can be discerned from migraine by 2 key factors: 1) attack duration is less than the 4-hour minimum duration of a migraine attack according to ICHD-II criteria (CH attacks last 15–180 minutes); and 2) restlessness is present in CH attacks. Migraine attacks are accompanied by avoidance of movement; CH attacks by pacing and other manifestations of agitation.

When an attack of CH or another TAC occurs, the posterior hypothalamus is activated, causing a disruption in the connections for sleep. Thus, CH attacks frequently wake patients out of sleep.3 Finally, the clinician should not be distracted by migrainous symptoms—phosphophoria can occur in 91% and phonophobia in 89% of CH attacks, and nausea occurs frequently in cluster as well.4

All CH sufferers need more than one acute treatment for attacks in case one fails. Because of the abruptness of the attack and its severity, as well as the short duration, oral medications should be avoided—they are too slow.

An extremely effective treatment to terminate a cluster attack is 6 mg of subcutaneous sumatriptan, achieving relief in 74% of patients within 15 minutes of onset vs placebo, and this formulation and dosage is Food and Drug Administration–approved for cluster.5 Sumatriptan nasal spray at 20 mg has also been shown to be effective in randomized controlled trials, and 5 mg zolmitriptan nasal spray has also demonstrated efficacy vs placebo.5

All patients should be given a portable 100% oxygen tank for acute treatment, and O2 becomes the first line therapy if triptans are contraindicated. A non-rebreather mask is used at a flow rate of 7–15 L for 20 minutes and can be repeated safely without issue.5 Other effective abortive treatments include IV, IM, or subcutaneous dihydroergotamine, possibly intranasal lidocaine, and blockade of the ipsilateral greater occipital nerve.2

Many patients will present with a sense that a cluster cycle or period is beginning, and will know

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Disclosure: Author disclosures are provided at the end of the article.
when attacks are starting. This is an excellent time to begin prophylactic therapy, which should be increased quickly but carefully until the majority of attacks have ceased. Otherwise, prevention is added as soon as the patient notes the cluster period has begun. Prevention might not be needed if at the end of a cycle.

The mainstay of preventive therapy is verapamil. It is typically tolerated up to 480 mg a day, although higher doses can be necessary. Patients can experience constipation, palpitations, peripheral edema, hypotension, and bradycardia. It is recommended that patients have an EKG with each significant increase in dosage.6

Because verapamil has significant side effects at higher doses, and because tachyphylaxis tends to occur with monotherapy, many headache specialists use a second preventive at the initial onset of treatment. Other drugs that can be effective include lithium, divalproex sodium, gabapentin, topiramate, methysergide, and, occasionally, melatonin (for episodic CH), or nasal capsaicin.7-10

Transitional treatment should be provided on the first visit while preventive medications are initiated, typically for 1–2 weeks. Corticosteroids can be used, beginning with 60–80 mg of prednisone daily and tapered by 20 mg every 3–4 days. Ergotamine tartrate at 2 mg or dihydroergotamine injection at 1 mg daily can be used effectively as well but preclude use of triptans for 24 hours after use.5

**PAROXYSMAL HEMICRANIA AND SUNCT/SUNA Pearl.** All patients with suspected PH or SUNCT/SUNA need to have an MRI of the brain with and without gadolinium.

**Oyster.** Patience with the patient is necessary as multiple medications may need to be tried before finding one that is effective.

PH and SUNCT/SUNA are characterized by multiple daily attacks of unilateral head pain with cranial autonomic features. As with cluster, PH comes in 2 forms: an episodic form, in which attacks occur in periods lasting 1–3 months followed by times of remission and recurrence; and a chronic form without a month of remission during a year. Chronic PH is more common.

Attacks of PH last 2–30 minutes, and occur more than 5 times per day at least half the time. Attacks can be differentiated from CH in that they are shorter, 50% of patients will not experience the restlessness that comes along with CH, and the patients may not be awakened from sleep. PH occurs more often in women; CH in men.

The best diagnostic marker for PH is the excellent response to indomethacin. We typically begin 25 mg of indomethacin 3 times a day and increase every 2–3 days until 75 mg TID is reached (if needed). This should be tapered every so often to see if remission has occurred, as the natural progression of PH is largely unknown.7 Other medications reported with occasional success include verapamil, celecoxib, acetazolamide, lithium, oxygen, ergotamine, and prednisone.11

SUNCT/SUNA is similar to PH but attacks last only 5–240 seconds (average 10–60 seconds) with up to 200 attacks per day.
Whereas CH, PH, and hemicrania continua (HC) occasionally occur without autonomic symptoms, SUNCT/SUNA attacks are defined by these features.\textsuperscript{11} SUNCT/SUNA can be differentiated from trigeminal neuralgia (TN) by the V<sub>1</sub> distribution (<10% of TN), the absence of triggers, the higher frequency of attacks per day, and the presence of autonomic symptoms.\textsuperscript{11}

SUNCT and SUNA may be refractory to treatment. Because the attacks are so short, therapy must be preventive. Lamotrigine (especially for SUNCT) and gabapentin (especially for SUNA) are the 2 most efficacious medications reported, but topiramate, intranasal lidocaine, corticosteroids, and IV phenytoin have been used as well.\textsuperscript{12}

Imaging of the brain is required when suspecting PH or SUNCT/SUNA, as there are secondary causes that when treated, may resolve these conditions. Reported MRI findings of cerebellopontine angle tumors, prolactinomas, meningiomas, venous angiommas in the brainstem, lacrimal gland retention cysts, and brainstem infarctions have all been described as causing secondary TACS, with pituitary tumor resection occasionally associated with cure.\textsuperscript{11}

DIFFERENTIAL DIAGNOSIS Pearl. Hemicrania continua is a unilateral headache with similar autonomic symptoms but is constant and responds well to indomethacin.

**Oyster.** Cervicogenic headache can be a mimic of HC, particularly in the elderly.

HC is a continuous, unilateral, moderate level side-locked headache with severe exacerbations of variable duration manifesting at least one ipsilateral cranial autonomic symptom. HC is probably much more common than originally thought and often misdiagnosed.\textsuperscript{4}

HC can also be accompanied by idiopathic stabbing headache, often called “jabs and jolts,” and is frequently associated with an ipsilateral foreign body sensation in the eye, like an eyelash or grit.\textsuperscript{13,14} MRIs of the brain are mandatory during the workup, as secondary HC has been reported, often with etiologies similar to secondary PH and SUNCT/SUNA.

Response to indomethacin is a diagnostic marker in HC, as with PH.\textsuperscript{15} Other medications occasionally reported as successful include other nonsteroidal anti-inflammatory drugs, gabapentin, lamotrigine, corticosteroids, dihydroergotamine, lithium, and melatonin.\textsuperscript{11}

Cervicogenic headache can mimic almost any headache, especially a TAC, and should be considered when there is lack of response to treatment. Unilaterality of pain, radiation from the neck, and failure to meet ICHD-II criteria for primary headaches can suggest cervicogenic headache as an alternative diagnosis to a TAC. Occipital nerve blocks can be helpful in cervicogenic headache, with physical therapy for maintenance, although Sjaastad et al. suggested controlled C2–3 blocks for diagnosis.\textsuperscript{16}

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REFERENCES
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Residency Training

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

Ivan Rocha Ferreira Da Silva, MD
Joao Antonio Gomes, MD

Neurology is traditionally recognized as primarily an outpatient or consultative specialty, usually attracting candidates whose main focus may not necessarily be the management of complex critically ill patients or the performance of invasive procedures. However, the advent of modern mechanical ventilation and, more recently, effective therapies for the treatment of acute ischemic stroke and other neurologic catastrophes is bringing about a paradigm shift, with neurologists increasingly assuming a more aggressive attitude and rapid response to frequently disabling and often fatal pathologies.

Neurocritical care has been around since the dawn of human civilization, and the Edwin Smith Surgical Papyrus already described many conditions considered to be under its scope, including head and spinal injuries, tetanus, and status epilepticus. The outbreaks of paralytic polio in the first half of the 20th century formally marked the first time that neurologists cared for critically ill patients, and the development of the iron lung used in the treatment of polio victims led to improved survival and served as a precursor to modern mechanical ventilation.1 Walter Dandy with a pioneer vision established in 1932 at the Johns Hopkins Hospital the first dedicated postoperative neurosurgical unit, recognizing the need for special care in sicker neurologic patients.2 Since those early days, the presence of neurologists in the critical care setting has grown exponentially. Modern neurocritical care is considered to have started with the organization and establishment of dedicated neurocritical care units (NICUs) during the 1980s with the work of Dan Hanley at the Johns Hopkins Hospital, Matthew Fink at Columbia University, Allan Ropper at Massachusetts General Hospital, and Thomas Bleck at University of Virginia at Charlottesville.3

There was an urge for improved care of critically ill neurology and neurosurgery patients, with needs not usually recognized and/or addressed in general critical care units. Specialized monitoring and highly trained multidisciplinary teams were also recognized as crucial pieces of this intricate mechanism. During the following decades, the exponential growth of clinical and experimental studies, the development of advanced methods of brain monitoring, and the creation of training centers led to a widespread establishment of these highly specialized units throughout the world.3

Caring for patients with neurologic and neurosurgical emergencies can be a challenging prospect that requires a unique set of skills. Many of these disorders rank among the most common causes of death and disability in the adult population and neurologists can expect to be frequently confronted with the care of patients afflicted by neuromuscular diseases (i.e., myasthenia crisis and Guillain-Barré syndrome), hypoxic-ischemic encephalopathy following cardiac arrest (for initiation of induced hypothermia and prognostication), status epilepticus, neurologic complications of medical diseases, meningitis, increased intracranial pressure, and the ubiquitous cerebrovascular diseases, among others. Moreover, neurologists should also be able to promptly recognize clinical deterioration in a given patient, initiate early interventions that may help limit the extent of neurologic injury, and urgently and efficiently triage patients to the intensive care unit.

Most physicians who lack a background in neurology are not comfortable managing critically ill neurology and neurosurgery patients and usually prefer to seek transfer of care to a facility with a dedicated NICU or rely heavily on their neurology consultants. Furthermore, although most large academic centers in the United States have a dedicated NICU, there remains a significant shortage of neurointensivists (i.e., only about 550 board-certified neurointensivists as of 2011 in the United States according to the United Council for Neurologic Subspecialities), and for the foreseeable future at least, neurology consultants should expect to have a major role in the management of this patient population, particularly during the early period of their disease process.4 The most recent census of the American Academy of Neurology (AAN)5 revealed that 37% of AAN members have their practices focused on cerebrovascular diseases, and approximately 10% on critical care. Also, more than half of the 54%

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of the members who consider themselves to be general neurologists work in large groups or hospital centers. We can therefore infer that a significant number of neurologists in the United States are likely consulted to help manage critically ill patients on a frequent basis and ample exposure to neurocritical care during residency training would serve to better prepare general neurologists for this task.

Although neurology consultants have an extremely important role in supporting the care of patients with neurologic diseases or complications in medical and surgical ICUs, neurointensivists have a broader training, including skills with invasive procedures, airway management, imaging analysis, and multimodal monitoring training. A growing body of literature supports that patients with traumatic brain injuries, ischemic strokes, intracerebral hemorrhages, and subarachnoid hemorrhages all have better outcomes and shorter hospital stay when treated by physicians with neurocritical care training. In an effort to disseminate the knowledge of basic neurocritical care competencies, the Neurocritical Care Society developed the Advanced Cardiac Life Support course, with the same guiding principles of the Advanced Cardiac Life Support training. The course aims to prepare the provider to promptly recognize and adequately treat the most frequent, disabling, and fatal neurologic conditions, based on current literature evidence.

Clinical rotations for neurology residents in the NICU can be an exciting experience, because they are often able to directly manage high-acuity patients under controlled conditions and adequate supervision. Although the learning curve can be steep at first, the progressive acquisition of knowledge and skills can prepare residents to recognize and promptly react to the most common presentations and complications of a great variety of neurologic emergencies. The Accreditation Council for Graduate Medical Education requires that neurology programs provide "exposure to and understanding of evaluation and management of patients in various settings including an intensive care unit and an emergency department with neurologic disorders and for patients requiring acute neurosurgical management." Similarly, the AAN states in the suggested core curriculum for neurology programs that "it is anticipated that experience in managing critically ill patients suffering primary or secondary neurologic dysfunction will occur throughout the three years of residency training in the intensive care unit, the emergency department and in-patient settings. It would be expected that there are discrete rotations in critical care and supplemented by didactic lectures/seminars by faculty and relevant correlations with other related areas." Nonetheless, the implementation of resident work hour restrictions poses new challenges that may negatively impact the feasibility and/or quantity of critical care exposure for neurology residents during their residency training.

A recently conducted survey supported by the AAN queried program directors of 132 neurology residency programs in the United States about the intensity and quality of the exposure of residents to neurocritical patients. A dedicated NICU was available in 64% of the programs, but only 56% of them offered a dedicated rotation in the NICU. The rotation was mandatory in 91% of the programs with a NICU and lasted an average of 4 weeks. According to this survey, the number of programs having at least 1 resident matching into a neurocritical care fellowship increased from 14% to 35% between 2005 and 2010. The study also identified factors that increased the likelihood of participating in a neurocritical care rotation during residency, such as the availability of a dedicated NICU, the presence of neurology-trained intensivists, availability of a neurocritical care fellowship, and a higher number of neurology residents per class.

The Neurocritical Care Society is committed to promoting education and training in neurocritical care and on its website it provides information about various elective programs in large academic centers available to residents and medical students. Moreover, a rotation in the NICU can be inspiring for many residents, attracting some of them to pursue a fellowship in the field. Neurocritical care is an ever-growing specialty, with exciting research opportunities in many areas of acute brain injury and a high demand for neurointensivists in large private and academic centers.

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Ivan Rocha Ferreira da Silva, first author, contributed drafting/revising the manuscript for content, including medical writing for content. Joao Antonio Gomes, contributing author, contributed drafting/revising the manuscript for content, including medical writing for content.

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Residency Training: Developing a program of quality and safety to train resident neurologists for the future

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ABSTRACT

Attention to quality and safety metrics is increasingly important for all physicians in practice due to mandates by governmental organizations, insurers, the public, and accreditation bodies. Neurology resident trainees need to acquire these skills, but little research in and outside of neurology provides guidance as to how to teach these important concepts. In the setting of new requirements mandating that training programs address these topics, we propose a number of strategies that can be implemented immediately in neurology residency training programs and call for increased investigation and sharing of best practices in order to adequately prepare neurology residents for the current and future environment of practice. Neurology® 2012;78:602-605

Quality care is defined by the Institute on Medicine as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge." Many practicing physicians have traditionally viewed "quality care" as a more nebulous concept ("I know it when I see it") that is difficult to recognize and challenging to apply to their own practice.

Measurement of quality usually involves examining structures, processes, and outcomes. Structures (e.g., having a neurologist examine any patient presenting with acute stroke) are easy to measure but are time and resource intensive to implement. Processes (e.g., prescribing an antiplatelet medication on discharge for secondary stroke prevention) have been the focus of the majority of quality research and policy to date. Outcome measurement, although desirable, has been fraught with difficulties including obtaining consistent longitudinal measurements in systems with multiple tiers of health service coverage as well as patient-specific variables (e.g., medication adherence) that are beyond the control of the individual physician. Much of the quality literature has been criticized by some for concentrating on these more easily measured structures and processes as opposed to clinically meaningful outcomes, a vital issue to address in future studies.

Neurologists will be increasingly expected to demonstrate that their care is of high quality, not only by hospitals justifying the expense of physician support, but also by insurers, governmental agencies, and a public increasingly engaged in a discussion emphasizing the delivery of high-quality care.

In the late 1990s, hospitals in the United States began to track core measures thought to represent quality care. This reporting is increasingly accessible to the public, even down to physician-specific details. Neurologists certainly will be asked in the near future to measure non-neurologic aspects of patient care that hospitals are required to report. Examples include rates of appropriate deep vein thrombosis prophylaxis and hospital-acquired infections. Focusing on these non-neurologic metrics is foreign to many neurologists, and adoption and dissemination of these good practices will be an important goal for our field. Physicians are increasingly rewarded and incentivized for good quality care, through these reporting metrics and even financial incentives such as "pay for performance" packages. Ultimately, neurologists of the future will need to be attentive to neurologic quality metrics that are only beginning to be defined.

Patient safety has also become a major focus for regulatory agencies, clinicians, and the public, stemming from the now decade-old Institute of Medicine report "To Err is Human." National patient safety goals are transforming medicine, with hospitals reporting and tracking "never events" and so-called "preventable con-

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References e1–e9 are available on the Neurology® Web site at www.neurology.org.
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ditions,” each of which carries financial and regulatory penalties. Building a “culture of safety” has become the mantra in medicine with analogies to the airline industry.

Quality and safety issues have become a major part of each practicing clinician’s daily routine and these influences are destined to expand. Despite the need to teach trainees these principles and prepare them for this new practice environment, there remains a dearth of relevant research on the topic within neurology. The Accreditation Council for Graduate Medical Education’s (ACGME) required core competencies of practice-based learning and improvement and systems-based practice hinge on trainees using quality and safety concepts to improve their own patient care and that delivered by the health care system. The ACGME milestones project will add depth to core competencies by establishing specific behaviors and accomplishments that are necessary for each trainee to reach proficiency in each competency.

Trainees not only need to learn these skills, but they will need to be maintained, refined throughout their career to maintain board certification. The American Board of Psychiatry and Neurology’s Maintenance of Certification Program emphasizes these concepts through performance in practice (PIP) requirements wherein physicians need to participate in quality improvement (QI) programs throughout their 10-year recertification cycle.

Systematic reviews of teaching QI and safety reveal that only a few studies to date describe interventions that target residents. The results of teaching these topics to medical students and other health professions mainly have demonstrated improved knowledge regarding quality issues when a group is tested after a didactic intervention. What is lacking is proof that these interventions have meaningful clinical benefits. While some studies show improvement in a process, these benefits tend to wane over time and do not become ingrained as permanent solutions, especially in the world of residency education where thoughful quality interventions may not be sustained when the resident “champion” graduates. This is a major challenge for resident QI projects and raises the stakes for systematic and effective involvement of residency program directors.

In the context of these challenges, we propose ideas by which neurology training programs can begin to teach quality and safety to residents within the limited confines of a training environment that is increasingly time challenged due to duty hours constraints and mandates to expose residents to an ever-widening set of clinical, administrative, and research experiences (table).

MAKE TEACHING QUALITY AND SAFETY A REQUIREMENT The ACGME common program requirements, which apply to all training programs regardless of specialty, were updated in 2011 to include language requiring programs to analyze clinical practice using QI methods and to initiate changes with the goal of improving patient care. Residency programs are also required to have their trainees identify systems errors and implement solutions. Participating in QI and safety programs is now a requirement for our trainees and necessary for residency and fellowship programs to maintain accreditation.

Internal medicine residents have been required by the ACGME to participate in a continuous QI process as part of their continuity clinics since 2009. This requirement has led to a number of successes and challenges that can inform neurology programs. The American Board of Internal Medicine’s Practice Improvement Modules (PIM) have been used as a tool to teach QI principles to residents. For example, one PIM instructs residents on evidence-based preventive medicine topics such as when to order screening colonoscopies; residents can examine their own clinical behaviors before and after this module. A similar approach in neurology could be successful in the setting of the American Academy of Neurology’s (AAN) recent publication of outpatient guidelines for quality care in various subspecialties.

Ultimately, a successful program for teaching quality and safety will need to establish interventions that make a demonstrable difference to patient care outcomes and are sustainable over time. The University of Chicago’s internal medicine program recently focused on developing this sustainability through the use of multiple cycles of a “plan, do, study, act” structure both early and late in the training program.

INCENTIVIZING QI GOALS In some institutions, resident incentives are used to encourage program-wide QI. At UCSF, the GME resident council sets institution-wide goals for the residents (e.g., all residents will improve their collective handwashing rate to 85%). In addition, individual residency programs propose yearly quality improvement goals (e.g., the neurology residents will increase dysphagia screening rates in stroke patients to 90%). Each proposal is vetted through a campus-wide quality group and these measures are tracked monthly with GME administrative support, giving real-time feedback to the residents as to their progress. Residents are given a financial bonus at the end of the year only if the goal is met.

These programs encourage residents to work together toward a common goal with close supervision.
Table
Quality improvement examples in medicine and potential outcomes relevant to neurology training programs

<table>
<thead>
<tr>
<th>Description</th>
<th>Assessment used</th>
<th>Neurology-relevant outcomes</th>
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<tr>
<td>TOPS project; multidisciplinary teamwork training sessions and formation of unit-based safety teams including solicitation of daily patient goals</td>
<td>Standardized surveys of patient safety culture</td>
<td>Improvement in safety culture on neuroscience-based floors with residents taking the lead as part of multidisciplinary teams</td>
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<td>Trial of a self-directed curriculum in quality of care for internal medicine residents in an outpatient clinic including readings, weekly self-reflection with faculty members, and medical record audits</td>
<td>Self-reported behavioral changes as well as patient quality of care metrics such as improvement in hemoglobin A1c and LDL levels</td>
<td>Improvement in neurology-specific quality of care metrics such as those recently proposed in AAN outpatient quality guidelines for epilepsy and Parkinson disease</td>
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<td>Patient safety education program with monthly conferences in a family medicine residency program focusing on ambulatory adverse medical events</td>
<td>Medical event reporting attitudes and reporting behavior before and after intervention</td>
<td>Neurology residents using a similar program could increase their reporting of untoward events and “near misses” to departmental QI and M&amp;M committees in both outpatient and inpatient settings</td>
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<td>Used ABIM clinical preventative services practice improvement module (PIM) to incorporate longitudinal QI curriculum and projects into required ambulatory rotations among residents</td>
<td>Multiple resident-based QI projects resulted from this PIM, each with distinct assessments; one example assessed the frequency of inaccurate medication lists in the ambulatory medical record</td>
<td>Neurology-specific projects could focus on performance in practice modules used for maintenance of certification; accurate medication lists could be targeted in a similar project given the multiple drug-drug interactions with neurologic medications such as antiepileptic drugs</td>
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<td>Residents perform a “systems audit” for upcoming M&amp;M conferences; upon completion of the audit, residents can critically review a case with an adverse event, identify a systems issue that led to the adverse outcome, conduct a root-cause analysis, interview stakeholders, propose solutions, and calculate costs</td>
<td>Resident awareness of systems issues, resident views of the educational value of M&amp;M conferences, and actual institutional improvements that resulted from the systems audits</td>
<td>Neurology programs could focus on M&amp;M cases related to tPA administration or other neurologic emergency treatments in the hospital leading to systems improvements (e.g., decreased door to tPA time)</td>
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<td>Fellows in internal medicine subspecialties were taught root cause analysis (RCA) processes via didactic sessions and provided conducting an RCA involving an adverse medication event</td>
<td>Faculty assessment of RCA competency as part of an objective structured clinical examination</td>
<td>Neurology residents or fellows could learn RCA skills and apply them to formal review of adverse events in outpatient and inpatient settings</td>
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</table>

Abbreviations: AAN = American Academy of Neurology; ABIM = American Board of Internal Medicine; LDL = low-density lipoprotein; M+M = morbidity and mortality; tPA = tissue plasminogen activator; QI = quality improvement.

from program directors and local QI experts. However, one potential limitation is that some incentives chosen may be mere “low hanging fruit” selected to maximize the likelihood of success. Many goals set only address national mandates (e.g., handwashing rates) without measuring local patient outcomes that result (e.g., reduction in nosocomial infection rates). Additionally, financial incentives may only be useful to spark the initial change in behavior and may indirectly discourage sustainability; residents may no longer put effort into quality and safety processes once the financial incentive to do so has expired.

USE MORBIDITY AND MORTALITY CONFERENCES AS A QUALITY AND SAFETY TOOL. The morbidity and mortality (M+M) conference can serve as another method to engage residents in patient safety issues. Rather than using the conference to embarrass or “call out” mistakes, M+M conferences can be used in a blame-free manner to explore errors and “near misses” while developing systems-based methods to avoid similar future mishaps. A culture of discovery and sharing of errors is needed for these conferences to run effectively; too often senior clinicians focus conference presentations on fantastic diagnoses rather than exposing and learning from their own errors. Leadership in open disclosure and improvement goes a long way in setting the example for our young trainees.

Placing residents in leadership roles on departmental M+M committees also allows for the development of these important skills. In the medicine department at the Mayo Clinic, residents are assigned to an M+M conference in advance to perform a “systems audit,” identifying areas to both emphasize during the conference and to use in improving structures. In some programs, residents run their own M+M committee or conferences in an effort to discuss these issues in a low-stakes environment without faculty presence. These efforts make safety part of the culture of the residency program and hopefully lead to sustainable professional habits.

FOCUS OTHER CONFERENCES ON QUALITY AND SAFETY ISSUES. It may be also useful for residency programs to focus other traditionally didactic conferences on quality and safety issues. Presenting brief “safety vignettes,” either using local cases or those available on Web sites such as that of the Agency for Healthcare Research and Quality (AHRQ), can be a useful adjunct to conference time. Patient-centered conferences that focus on errors or “near-misses” can take the place of yet another didactic talk regarding a neurologic topic. In
some institutions, periodic “patient safety rounds,” where current inpatients are discussed with an eye exclusively on safety issues, can help address problems in real time, avoiding potential errors, and changing systems to provide safer care.

**USING ROOT CAUSE ANALYSES** Root cause analyses (RCAs) are another useful construct for trainees to learn about safety issues and develop systems-based solutions in the face of medical errors. Mandated by the Joint Commission, RCAs are advantageous because they are by nature interdisciplinary and focus on the “why” and “how” of errors rather than “who.” At the end of the process, structural changes are suggested to avoid similar mishaps going forward; these changes are usually not physician-specific, allowing trainees a window into the complex health care environment that allows for safe care within a multidisciplinary team. Ideas for success include resident-run departmental RCAs and placing residents on hospital-wide RCA committees.

**BUILDING A CULTURE OF SAFETY** Although safety and quality metrics are often viewed as overlapping with a blurred divide, the field of safety offers a number of unique learning opportunities. The concept of building a “culture of safety” is a broad one that involves teamwork and communication among diverse providers. Many of the already mentioned interventions help to achieve this goal. Residents can play a crucial role in developing this culture and be given the opportunity to play a leadership role, interacting with nursing, pharmacy, case managers, and even patients to achieve a common goal. The TOPS project is one such published multidisciplinary, inpatient unit-based system that engages residents in developing and maintaining a culture of safety and could be used on neuroscience-focused hospital floors.

**RESEARCH AND DISSEMINATION OF BEST PRACTICES** Given the impetus for teaching safety and quality education in neurology, residency programs need to recognize these issues as a major focus of training. Research within neurology is sorely needed and essential to the development of specialty-specific tools. Sharing best practices among programs is important as with any relatively new area of focus in education. Ultimately our trainees need to be prepared for a life in practice that continually examines QI and safety, a task in which the AAN will become an organizational hub. We must quickly develop the means to impart these skills during training or face a group of graduates ill-prepared for this aspect of the real world of neurologic practice.

**AUTHOR CONTRIBUTIONS** Dr. Josephson was responsible for the study concept/design and drafting/revising the manuscript for content. Dr. Engstrom was responsible for drafting/revising the manuscript for content.

**DISCLOSURE** Dr. Josephson serves as an Associate Editor of *Annals of Neurology* and *The Neurohospitalist*, and as Editor-in-Chief of *Journal of the White Neurologist.* Dr. Engstrom receives research support from the NIH.

**REFERENCES**

Right Brain

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

Pavan Bhargava, MD

Most of us tend to remember moments that define the major decisions in our lives, the events that make indelible impressions in our minds. In the monotony of our daily existence, remembering these moments helps give us perspective. It helps remind us why we do what we do. When I think back on the pivotal moments that pushed me to become a neurologist, I always remember a face—a smiling face of a young girl.

I was an internal medicine resident in the second year of my training in India. It was a day like any other: patients to see, procedures to complete, and notes to write. Everything was going as planned until I met her. She was a shy girl of 17. She had been sent in from the outpatient clinic to be admitted for evaluation of pyrexia of unknown origin (PUO). The intern and I began the usual process of evaluation—beginning with a history and physical examination. In my head were echoing the words of my department chair: “PUO needs a very thorough history and exam.” Determined to do a good job, I began the laborious process. She told us that she had been febrile for about 3 weeks. Besides this, we could elicit no other complaints. She answered in the negative to our massive inventory of questions. Then followed a physical examination, beginning literally with the head and ending at the toes. I thought I heard a faint murmur when I was listening to her heart sounds; however, in the noise of a busy medical ward, it was hard to be sure. I asked the intern to check and then another resident. Neither was sure they heard it. I decided to continue with the rest of the examination. Having always been fond of the brain, I did a full neurologic examination, including a fundus examination. At the end of this we had still not found anything abnormal.

Her initial laboratory tests had been unremarkable and we were stumped. It was then that it happened. My intern cracked a joke. I do not recall the details now, but I guess it must have been funny because it elicited a smile from the patient. It was a peculiar smile—because it most definitely was lopsided. Having seen this, I proceeded to repeat the cranial nerve examination. I asked her to grin and to show her teeth, both of which she did perfectly well. I was puzzled. I was sure there had been asymmetry in her smile just a few seconds ago. Observing her a little longer, I noticed it again: when she smiled spontaneously, one side of her mouth did not move as well as the other. We questioned her relatives and they confirmed that this was not something they had ever noticed before. It was still a puzzle to me: she could grin symmetrically when I asked her to, but when she smiled spontaneously, she had weakness of one side of her face. A trip to the library revealed that I was dealing with an emotional facial paralysis.1 From my reading, I learned that the pathways controlling voluntary and emotional facial movements were separate.2 The pathway controlling emotional facial movements began in the supplementary motor area or the cingulate cortex and via the anterior portion of the internal capsule and thalamus ultimately reached the facial nucleus in the pons.3

Armed with this new knowledge, I proceeded to order an MRI of the brain. An MRI was something that could not be ordered lightly in a resource-poor setting like India. The MRI confirmed that she had a thalamic stroke, which had in the literature been described as causing emotional facial paralysis.4 We then proceeded to do an echocardiogram and established the diagnosis of subacute bacterial endocarditis. She was treated and recovered well.

That day I added a new tool to my neurologic bag of tricks—a sense of humor. From that day forward, I do not consider a neurologic examination complete until I make the patient smile.

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DISCLOSURE
Pavan Bhargava reports no disclosures. Go to Neurology.org for full disclosures.

REFERENCES

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Right Brain: The blind spot

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“He’s not moving his left arm.”

No mother wants to hear that about her newborn in the delivery room. I was a fourth-year medical student; my husband was a surgical resident. We couldn’t contain the windstorm of scary diagnoses that came over us as we heard those words. Did he have a congenital syndrome? A stroke? Over the next few days, the pediatricians reassured us it was “just a brachial plexus palsy” and we had nothing to be concerned about. The comment that put my motherly fears to rest: “I’ve never seen a case that didn’t recover.”

My delivery was complicated by shoulder dystocia and my son, Andy, was born with a brachial plexus birth palsy, giving him a flaccid left arm that had the characteristic “waiter’s tip,” with some movement in his fingers, but none in his arm. My heart ached every time I swaddled him and felt no resistance from his left arm. “Is there anything special we should do for him?” we asked before we left the hospital. The answer was always a reassuring, “No—we treat these children normally because they all end up getting better.” Four different pediatricians, no special exercises, no extra precautions, no additional visits. We were so relieved. Andy was a normal baby.

Over the next few weeks, my husband and I watched our son’s arm, but we were not overly concerned, trusting what we’d been told. Sure, Andy’s left arm was cooler than his right—but that would improve. Sure, his arm was atrophied—but it would catch up. Sure, it still wasn’t moving—but in time it would. A few days before his 2-month appointment, we noticed that there was an unusual smell about Andy. To our horror, we found a pressure ulcer on his wrist. Because of weakness from his brachial plexus injury, his wrist was adducted and not moving, so it had remained in the same position for 2 months, other than for the occasional bath. We had been told specifically that Andy did not need special care. The guilt … the feeling that we’d somehow neglected our baby to the point that he’d get a pressure ulcer produced a lump in my throat that didn’t go away for weeks.

That was the beginning of a new awareness for us—the realization that there was something our doctors didn’t know about Andy’s situation. For if they did know, we would have received anticipatory guidance on avoiding something as simple as a pressure ulcer in a newborn. With this new understanding, we were finally able to see what we had been subconsciously denying: Andy’s condition had not improved.

The next day, we went to Andy’s well-baby check-up. The pediatrician took one look at his arm and immediately the tension in the room was tangible. We didn’t want to hear what our doctor was saying, but the words “permanent functional deficit” slammed through our ear drums. That phrase kept reverberating in our heads. We had suspected that our son was not recovering as fast as he was expected to, but “permanent functional deficit” threw this game into a whole different arena. My thoughts were racing: Would Andy ever climb a jungle gym? Would other children tease him at school? Over the next few minutes, our pediatrician outlined a flurry of steps: referrals to neurologists, physical therapy, and resource centers for the developmentally disabled. How, we wondered, in 1 hour, could we have gone from a well-baby visit to a referral to services for the disabled?

We were devastated, bewildered, disappointed. We were devastated by what we imagined could be the future for our son. We were bewildered by how we, as medically sophisticated as we were, could have been so blind that we didn’t see the reality of Andy’s situation. We were disappointed in ourselves that we didn’t actively ensure that Andy was getting the appropriate care for his condition. Nevertheless, we were also grateful. We were grateful for the wake-up call.

The question that has revisited us over and over again was how at such a preeminent medical center our son could have fallen through the cracks. Over 90% of cases of brachial plexus birth palsy spontaneously recover within the first 2 months of life. Andy’s physicians had seen cases of brachial plexus birth...
palsy before; most likely, all of their patients had recovered. Could our doctors have been lulled into the assumption that all these cases got better, given the benign nature of their prior experience? Why had they not discussed with us that 10% of patients with these injuries don’t fully recover? What was the reason the worst-case scenario—complete nerve detachment (avulsion)—was never even mentioned?

Eventually, we realized that situations like ours are more likely to occur when, as treating physicians, we don’t know that we don’t know. When we do know, we try to provide the best possible care. When we don’t know, we readily admit our lack of knowledge and either refer to the literature or to our colleagues. It is when our gaps of knowledge fall into our brain’s “blind spot” that we get into trouble. Throughout my training in medical school, there was always an emphasis on expanding our fund of knowledge in areas we weren’t familiar with, whether that was going to grand rounds on new topics or looking up new diagnoses our patients had. The focus was on trying to expand the limits of what we didn’t know. Andy’s case reminds us that it is also necessary to explore the limits of what we do know—or more importantly, what we think we know. Whether it’s the repetitious element of becoming more experienced or the fact that what we learned at one point has become outdated, it is easy to slide into complacency. It is easy to think, “I have seen this diagnosis before; I know how to treat it.” This assessment would likely be accurate for most of the patients we see. The danger, however, is that complacency—and simply, the passage of time—widen our blind spot and make us overlook things we either once knew or should now know. Perhaps what distinguishes the great clinician from the good one is the ability to maintain a fresh outlook with each patient and to wonder whether a given patient is different from the rest. For what if the patient in front of you is the 10%: What if it happens to be the worst-case scenario? What if your patient is a rare presentation of the common—as Andy was—or a common presentation of the rare?

Challenging ourselves to explore the limits of what we think we know may not change the treatment plan or outcome ... most of the time. But then there are those critical moments when actively challenging the boundaries of our blind spot could mean the difference between a child being able to put his shirt on with both arms or putting it on with just one.

ACKNOWLEDGMENT
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REFERENCE
Teaching NeuroImages and Teaching Video 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: Brain mass with hilar adenopathy
The importance of histologic diagnosis

Figure 1  Brain and chest imaging

Coronal contrasted T1 (A) shows heterogeneously enhancing, multifocal mass. Axial fluid-attenuated inversion recovery (B) shows vasogenic edema. Chest x-ray (C) and CT (D) demonstrate lymphadenopathy (arrows).

Figure 2  Pathology

Lymph node biopsy (A) reveals sarcoid, with noncaseating granuloma (asterisk) surrounded by lymphocytes (arrow). Brain biopsy (B) reveals glioblastoma, with pseudopalisading necrosis (asterisk) and vascular proliferation (arrow).

Download teaching slides: Neurology.org

From the Division of Neuro-Oncology (J.T.J., S.R.P.), Department of Neurology (H.-S.Y., D.N.), Massachusetts General Hospital, Boston. Go to Neurology.org for full disclosure. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
A 30-year-old man presented with weeks of progressive headaches, imbalance, and aphasia. Brain MRI revealed an enhancing left frontal mass (figure 1, A and B). Chest imaging revealed mediastinal and hilar adenopathy (figure 1, C and D). Metastatic cancer was initially suspected, but pulmonary lymph node aspiration revealed sarcoidosis (figure 2A). Subsequent brain biopsy revealed glioblastoma (figure 2B).

This case emphasizes the importance of histologic diagnosis before initiating therapy. One study demonstrated nearly 50% variation in diagnosis following brain biopsy, 27% leading to a change in treatment. Sarcoïd is associated with increased risk of certain cancers, though this has not been demonstrated for gliomas.2

AUTHOR CONTRIBUTIONS
Analysis and interpretation of data: Drs. Jordan, Yang, Narendra, and Plotkin. Drafting of the manuscript: Drs. Jordan, Yang, and Plotkin.

REFERENCES

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DISCLOSURE
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A tasteless lesion

J.A. Feldman, MD; S.L. Galetta, MD; R.R. Miselis, VMD, PhD; A.C. Rosenquist, PhD; and B.M. Ances, MD, PhD

A 45-year-old restaurant owner noted loss of taste over his entire left tongue during a two-week time period. Neurologic exam was otherwise normal including facial strength. Brain MRI revealed an enhancing lesion of the left dorsal pons (figure, A and B). The patient subsequently developed coordination difficulties and double vision. Repeat MRI confirmed a left superior cerebellar and a new frontal white matter lesion consistent with multiple sclerosis.

The anatomy of the secondary projection fibers conveying the sensation of taste in humans remains poorly understood.1 Recent mapping studies in monkeys suggest that the second order neuron projections from the nucleus of the solitary tract pass through the dorsolateral pons before ascending as the central tegmental tract.2 The lesion in our patient is just above the nucleus of the solitary tract and lies in the location of the second order neurons that project to the thalamus for taste.

We conclude that the ascending taste fibers from the nucleus solitarius travel within the dorsolateral pons just medial to the superior cerebellar peduncle. A lesion in this location may produce this isolated deficit.

References

Figure. (A) Axial fluid level attenuation recovery MRI above the level of the nucleus of the solitary tract and (B) T1 postcontrast coronal at the pontomesencephalon. In both images, arrow shows demyelinating lesion.
Teaching Video NeuroImages: Semiology and localization of ballistic movements

Ballistic chorea (hemichorea–hemiballism) localizes to the subthalamic nucleus and its connections (video 1, figure, Aa) or the putamen (video 2, figure, Ab). Other large-amplitude hyperkinetic lesional movements can have similarly high localizing value. “Ballistic” tremor may develop months after recovering from ventrolateral thalamic strokes, in the thalamogeniculate vascular territory (video 3, figure, Ac and Ad). Similarly, “ballistic dystonia,” limb dystonia with superimposed arrhythmic and jerky movements often referred to as myoclonic dystonia, may develop months after recovering from combined vascular lesions in the striatum and posterior thalamus (video 4, figure, Ae and Af). These motor complications, delayed by hours to days (hemiballism) or weeks to months (ballistic dystonia and tremor), have relatively distinct localization value to a narrow “ballistic corridor” in the basal ganglia and thalamus (figure, B).

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REFERENCES
(Aa) Head CT in a patient with hemichorea-hemiballism due to subthalamic stroke. An area of hyperintensity restricted to the region in and around the subthalamic nucleus represents a hypertensive hemorrhagic stroke (video 1). (Ab) Axial T1-weighted brain MRI in a patient with hemichorea-hemiballism due to diabetic ketoacidosis. The area of T1 hyperintensity in the left posterior putamen was identified during an episode of severe diabetic ketoacidosis 3 weeks before the onset of right hemiballistic chorea (video 2). (Ac, Ad) Axial and coronal T2-weighted brain MRI in a patient with ballistic tremor. The area of T2 hyperintensity is restricted to the ventrolateral thalamus, corresponding to a stroke in the thalamogeniculate arterial territory (inferolateral arteries, P2) (video 3). (Ae, Af) Axial gradient echo brain MRI in a patient with ballistic dystonia. The regions of susceptibility artifact are due to hemosiderin deposition resulting from a remote hemorrhagic infarct involving the right posterior putamen, posterior thalamus, and upper midbrain, adjacent to the subthalamic nucleus (video 4). (Bac-c) Basal ganglia lesioned “corridor” of ballistic movements. The ballistic movements have localizing value (shown in red) by narrowing the lesion in or around the subthalamic nucleus (a, hemiballism), ventrolateral thalamus (b, ballistic tremor), and dorsolateral putamen and posterior thalamus (c, myoclonic dystonia or “ballistic dystonia”) (printed with permission: Mayfield Clinic).
Teaching Video NeuroImages: Complicated scapular winging

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Figure 1. Upper limb muscle MRI. T1-weighted sequences of the 2 sisters


Scapular winging (SW) is a common sign in neuromuscular disorders. Besides “pure” phenotypes due to single muscle weakness often secondary to nerve injuries or dysfunctions,1,2 the phenotype can be complicated when a combination of different scapular fixators is involved by a myopathy. We show an example of 2 sisters with facioscapulohumeral muscular dystrophy (video 1 on the Neurology® Web site at www.neurology.org). In patient 1, the SW is caused by an isolated trapezius weakness. Conversely, in patient 2, the left SW can be attributed on clinical grounds to a combined serratus anterior and trapezius weakness. Both hypotheses are confirmed by muscle MRI (figure 1).

AUTHOR CONTRIBUTIONS
M. Monforte and G. Tasca designed the study and drafted the manuscript. E. Ricci and E. Iannaccone collected the data and revised the manuscript for intellectual content.

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REFERENCES

From the Institute of Neurology (M.M., E.L., E.R.), Catholic University School of Medicine, Rome; and Don Carlo Gnocchi Onlus Foundation (G.T.), Milan, Italy.
E-Pearls of the Week

June 20, 2014: Parechovirus and Neurologic Disease

The advent of real-time reverse transcriptase PCR (RT-PCR) has allowed for improved detection of viral pathogens in meningitis and encephalitis. The human parechoviruses are an increasingly recognized cause of neurologic illness since the availability of commercial PCR testing. Parechovirus infection can result in a meningoencephalitis and has become a major pathogen in childhood, especially infants under three months of age (1). The prevalence of parechovirus in pediatric CSF samples ranges from 1–7%, and cases are not associated with significant CSF pleocytoses (2). Infections are seasonal, often occurring from late Spring through Fall (2). In comparison to CNS enterovirus infection, those with parechovirus are more likely to have altered mental status, seizures, and ataxia (2).

References:


Submitted by Adam Numis, MD.

July 8, 2013: HINTS of Stroke

The acute vestibular syndrome is characterized by rapid onset of vertigo, nausea, vomiting, gait instability, head motion intolerance, and nystagmus. This commonly encountered condition results from a variety of potential etiologies ranging from benign peripheral vestibular pathology such as labyrinthitis to more sinister central pathology such as brainstem stroke. Bedside evaluation showing normal head-impulse testing, direction-changing nystagmus on eccentric gaze, and skew deviation (i.e. Head Impulse, Nystagmus, Test of Skew; HINTS) has strong predictive value for brainstem stroke. (1) In contrast, bedside evaluation showing abnormal head-impulse test, unidirectional nystagmus, and absence of skew deviation excludes stroke better than an early negative MRI and strongly predicts peripheral pathology. (2)

References:


Submitted by Roy Strowd, MD, Resident Physician, Wake Forest School of Medicine, Winston Salem, NC.

Dr. Strowd is a member of the Resident and Fellow Section of Neurology.