The Seventh annual Highlights of the Resident and Fellow Section: 2014
A Representative Collection of Previously Published Articles

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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 28, 2014, 7:30 p.m.–9:00 p.m.  Philadelphia Marriott Downtown
Neurology® Resident and Fellow Section Writing Award

The winners of the 2014 Award are:

**Right Brain: A reading specialist with alexia without agraphia: Teacher interrupted.**

Jason Cuomo, MA, Murray Flaster, MD, PhD, and José Biller, MD

*Neurology* January 7, 2014 82:e5-e7

The winners will be honored at the 2014 AAN awards luncheon. See page 44 of this Highlights booklet for the award-winning article.

The *Neurology* Resident and 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 and 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 2015 and will be awarded for a paper published in 2014.

No formal application process is required. All manuscripts submitted to the section will be considered. Manuscripts should be submitted online at [neurology.org](http://neurology.org). Please direct any questions to kpieper@neurology.org.

### Past Recipients

**2013 Award Winner**

Daniel R. Gold and Stephen G. Reich
October 23, 2012 79:e146-e152

**2012 Award Winner**

Christina B. Pham, Johannes R. Kratz, Angie C. Jelin, and Amy Gelfand
August 16, 2011 77:695-697

**2011 Award Winner**

Amy Gelfand, MD
Right Brain: We were all once ‘fixed and dilated’.
November 16, 2010 75:1851-1852
The Neurology® Resident and Fellow Section was launched as a page in 2004 to provide a forum for trainees and educators to write about topics relevant to residency and fellowship, including academic research projects, practice, ethics, teaching, historical topics, and international training experiences. The “page” has since evolved into a major section of the journal, with articles appearing weekly. Though most are published on-line, exceptional articles also appear in the print journal. The number of submissions to the section has increased dramatically (from 12 in 2004 to 481 in 2013), and the quality of published manuscripts has improved (represented by our current acceptance rate of about 23%). We published 165 manuscripts in 2013, our highest number to date.

Neurology Resident and Fellow Section Submissions and Acceptances 2004-2013

![Graph showing Resident and Fellow Section Submissions and Acceptances 2004-2013](image)

The Resident and 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 of interest to trainees. Residents will be selected annually, with requests for applications occurring in the Spring. This provides an opportunity for these trainees to begin a process of lifelong learning about writing, reviewing, and identifying articles of importance to the field. Section members also write articles, but the vast majority of manuscripts are written by neurology trainees, program directors, and educators around the world.

The Section has several different subsections, many are represented by the articles in this booklet. These include Emerging Subspecialties in Neurology, Clinical Reasoning, Right Brain, Child Neurology, Journal Club, Pearls, and Oy-sters, International Issues, Education Research and Initiatives, Teaching Neuroimages (including both static images and videos), and Book and Media Reviews.

The group has also initiated and developed numerous other unique projects since the inception of the Section, including a website, podcasts, weekly electronic communications, an annual writing award, Mystery Cases, Call for Authors, and other new subsection ideas. Podcasts related to articles published in the RFS began in December 2007, for example, and weekly E-Pearls, now archived on our website, have been sent to residents nationwide since July 2008. The first annual RFS writing award was awarded in April 2009, the first Mystery Case published in August 2009, our website launched in 2010, and the first journal club articles published in August 2011. In 2011, we expanded our book review section to a new Media and Books Reviews Section to provide reviews of other forms of educational media in increasing use, including websites and apps. 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 available all Teaching Neuroimages as teaching slides. In 2014, we plan to begin work on the first of our E-books, which will be focused on metabolic diseases.

We hope you enjoy this year’s edition of the Highlights of the R&F!

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

John J. Millichap, MD, Deputy Associate Editor, Resident and 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 healthcare policy, cost-effective utilization, and medical education.

Jeremy Gregory, MD

Jeremy Gregory studied biochemistry, biophysics, and Spanish at Oregon State University and then medicine at Mayo Medical School. He is currently a resident in the adult neurology program at Mayo Clinic in Rochester, Minnesota. His academic interests include movement disorders, prion diseases, art in medicine, and teaching and education research.

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 subspecialty training in pediatric stroke followed by an academic child neurology practice with a focus on medical education at the student and resident level.

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. Her thesis was completed in the Pittsburgh Center for Pain Research where she investigated ion channel mechanisms of dual afferent sensitization in migraines using patch clamp electrophysiology. Recent research endeavors include investigating the association between genetic variants, migraine and stroke risk. She continues to pursue translational and basic science research with academic interests in headache and stroke. She enjoys teaching, community outreach, and mentoring.

Audrey Brumback, MD, PhD

Audrey Brumback earned her MD and PhD degrees from the University of Colorado School of Medicine, where she studied the role of cholesterol transporters in neocortical seizures. She completed Child Neurology residency at the University of California, San Francisco in 2012, and is now an assistant professor in the Division of Child Neurology. She was fortunate to receive funding from the NINDS R25 program to perform research during residency and is now funded by a K12 through the NICHD. Her current research focuses on mechanisms of electrophysiological dysfunction in the autistic brain.

Joseph Cahill, MD

Joseph Cahill is a third-year neurology resident at the University of Wisconsin. He attended medical school at the Universidad Autonoma de Guadalajara in Guadalajara, Mexico, after serving eight years as an active duty Hospital Corpsman in the US Navy. He can now say he is a bilingual, bicultural physician. He is also a screenwriter whose credits include Manipulating Life, a short film produced in 2008 that was shown in festivals around the US. He has yet to write that Oscar-winning feature film. He is currently serving as an active duty Navy Lieutenant and plans to retire at a young age somewhere off the coast of Mexico. His other interests include traveling and competitive beach volleyball.

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, and went on to investigate mouse models of neonatal hypoxic ischemic injury in the pediatric neurology department of the University of California, San Francisco before attending medical school. She graduated from the Keck School of Medicine of the University of Southern California and completed her pediatric training at Children’s Hospital Los Angeles. Her interests include pediatric movement disorders as well as behavior and development.

Daniel Goldenholz, MD, PhD

Daniel Goldenholz completed his MD PhD training at Boston University, where his thesis work focused on multimodal imaging techniques for brain mapping and epilepsy. He then completed a one-year post-doctoral fellowship at the Harvard/MIT/MGH Martinos Imaging Center, studying techniques in fMRI, DTI, TMS, and near-infrared spectroscopy. He completed his internship in medicine and residency in neurology at Alameda County Medical Center and UC Davis Medical Center. He is currently pursuing a clinical epilepsy fellowship at the NIH.

Andrea Millichap, MD

Dr. Millichap is an avid writer himself and enjoys an active volunteer role in the field of medicine. 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.
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<td>Fourth-year resident at the University of Ottawa</td>
<td>Adult neurology, functional connectivity, functional neuroanatomy</td>
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<td>Matthew R. Lincoln, MD, DPhil</td>
<td>Third-year resident at the University of Toronto</td>
<td>Multiple sclerosis, genetics of multiple sclerosis, multiple sclerosis and the history of neurology</td>
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<tr>
<td>Andrew Schepmyer, MD</td>
<td>Resident at the University of British Columbia</td>
<td>Neuroregeneration, neuroimmunology, and neuromuscular disorders</td>
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<td>Craig Press, MD, PhD</td>
<td>Child neurology resident at the University of Colorado Denver</td>
<td>Biomedical engineering, neurodegenerative diseases, gene therapy</td>
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<td>Peter Pressman, MD</td>
<td>Resident at Oregon Health Science University</td>
<td>Neurointensive care, sleep medicine, epilepsy, neurophysiology, pediatric neurocritical care, and traumatic brain injury</td>
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<td>Matthew Lincoln</td>
<td>Resident at the University of Toronto</td>
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<td>Sara Stern-Nezer, MD, MPH</td>
<td>Resident at the University of Toronto</td>
<td>Multiple sclerosis, genetics of multiple sclerosis, multiple sclerosis and the history of neurology</td>
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*Note: The table continues with similar entries for other individuals.*
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 NeuroImage now 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 R&FS 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 R&FS reviews neurology apps and other electronic media.

6. The Right Brain subsection explores the relationship between neurology and the humanities, and is good tool to encourage reflection among residents.

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 R&FS. 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 R&FS on Facebook: join our group entitled ‘American Academy of Neurology Residents and Fellows.’ For further digital access to R&FS 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 R&FS regularly, send us manuscript submissions, and apply for a position on our editorial team during our annual recruitment!
Child Neurology

The Child Neurology Section in the Resident and 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.
Organic acidurias are an important group of inherited metabolic disorders that affect the intermediary metabolic pathways of carbohydrate, amino acid, and fatty acid oxidation, leading to the accumulation of organic acids. The 2-hydroxyglutaric acidurias are rare neuro-metabolic disorders characterized by developmental delay with or without other neurologic dysfunction. Three different subtypes have been described: D-2-hydroxyglutaric aciduria, 1-2-hydroxyglutaric aciduria, and combined D,L-2-hydroxyglutaric aciduria. We describe the case of a child presenting with developmental delay who was found to have the classical biochemical, imaging, and genetic features of 1,2-hydroxyglutaric aciduria.

Case report. A 7-year-old girl presented to the clinic for evaluation of cognitive delay. The patient, born at 41 weeks gestation, appeared to have met her early milestones on time. Her parents first became concerned about her development at approximately 4 years of age, when she was noted to have difficulty focusing and keeping up with her peers. Teachers described her as easily distracted and forgetful. Over the years, it was noted that she was increasingly lagging behind academically. Developmentally, when she was seen in clinic at age 7, she was able to ride a bike with training wheels, write her name and draw pictures, and dress herself. Her speech was difficult to understand.

She had a history of 3 convulsive febrile seizures at a younger age. Otherwise, she had not been noted to have any cognitive or neurologic decompensations with intercurrent illnesses. There was no family history of seizures or developmental delay. Her parents are originally from a small village in Eritrea and they denied any consanguinity.

On examination, her head circumference was 53.7 cm, at the 98th percentile. Weight and height were at the 50th percentile. She was able to state her name but was unable to recall the day of the week or month. She was able to follow a 2-step command, repeat 3 digits forward, and print her name legibly, but she had difficulty with right/left differentiation, subtracting, and reading. Her speech was suggestive of a lingual dysarthria, with about 25%-50% of her speech understandable to the examiner. She had mildly decreased tone throughout and had difficulty hopping or standing on each foot. Though her gait was normal, she was unable to tandem gait. The rest of her neurologic examination was normal for age.

**What would her developmental age be based on the description given above? Would you consider brain imaging as part of the workup for developmental delay in a child?**

Her developmental skills were approximately in the 4- to 5-year-old range. As part of the American Academy of Neurology (AAN)-recommended workup for children with developmental delay, an MRI of the brain was done (Level B; Class III evidence). This showed extensive relatively symmetrical white matter (WM) hypointensity involving mostly the subcortical WM (figure). There was relative sparing of the periventricular and perirlandic WM. Both the caudate and lentiform nuclei showed abnormal signal with sparing of the thalamus. The dentate nuclei showed similar increased signal intensity. There was sparing of the corpus callosum and brainstem.

**What conditions can produce this MRI pattern of WM involvement or abnormal signal in the basal ganglia? What would be the next step in your workup?**

The differential diagnosis for the imaging findings discussed above would include Canavan disease, Kearns-Sayre syndrome, 3-hydroxy-3-methylglutaryl-coenzyme A lyase deficiency, and succinic semialdehyde dehydrogenase deficiency.

Bloodwork performed included a normal thyroid-stimulating hormone level, plasma pyruvate, lactic acid, amino acid screen, total/free carnitine levels, and acylcarnitine profile. Urine was sent for analysis of organic acids and the results showed “massive excretion of 2-hydroxyglutaric acid” (>1,000 mmol/mol creatinine). At this point genetic testing was performed, showing a homozygous mutation in the 1,2-hydroxyglutarate dehydrogenase gene. The mutation consisted of a T>G transversion (c. 903T>G) in exon 7, resulting in the substitution of tyrosine by a stop codon at position 301 (p.Tyr301X). Based on these
results and clinical presentation, a diagnosis of L-2-hydroxyglutaric aciduria was made.

**DISCUSSION** The algorithm to evaluate children presenting with global developmental delay varies case by case. In our case, an MRI of the brain was performed as the initial investigation after confirming that the newborn metabolic screen was negative. This was based on the AAP guidelines for the evaluation of children with global developmental delay, which state that the diagnostic yield of neuroimaging increases in the presence of physical findings (in our case macrocephaly, dysarthria, decreased tone, and ataxia) (Level C; Class III evidence).2 After obtaining the MRI of the brain, urine organic acid levels were sent. It was only at this point that genetic testing was performed to confirm the diagnosis of L-2-hydroxyglutaric aciduria.

L-2-Hydroxyglutaric acid is generated from an NADPH-dependent conversion of 2-ketoglutaric acid in a reaction catalyzed by l-malate dehydrogenase, a mitochondrial enzyme in the tricarboxylic acid (TCA) cycle. L-2-Hydroxyglutaric acid has no known function in humans and this reaction is thought to be an unwanted side reaction of l-malate dehydrogenase. L-2 Hydroxyglutarate dehydrogenase is the enzyme that prevents the loss of these carbon moieties from the TCA cycle and also protects from toxic accumulation of L-2-hydroxyglutaric acid by irreversibly converting it back to 2-ketoglutaric acid with flavin-adenine dinucleotide as a coenzyme, acting as a “housecleaning” enzyme for this unwanted side reaction.4 The biochemical hallmark of L-2-hydroxyglutaric aciduria is the accumulation up to 300 times control values of urinary L-2-hydroxyglutaric acid. L-2-Hydroxyglutaric acid levels are also elevated in the plasma and CSF.5

Pathogenic mutations of L-2-hydroxyglutarate dehydrogenase causing L-2-hydroxyglutaric aciduria were first identified in 2004, with the majority of the variants being missense mutations that alter invariably conserved amino acids.6 The L-2-hydroxyglutarate dehydrogenase gene has been mapped to chromosome 14q22.1. L-2-Hydroxyglutaric aciduria is inherited in an autosomal recessive fashion with 88 unique DNA variants being reported as of March 2012 in the Leiden Open Source Variation Database (http://www.LOVD.nl/L2HGDH). However, not all of these 88 DNA variants have been proven to be pathologic. In our case, genetic testing confirmed that the clinical syndrome was secondary to a mutation in exon 7 of the L-2-hydroxyglutaric aciduria gene. Though missense mutations are more commonly described, nonsense mutations, as in our case, have also been found to cause L-2-hydroxyglutaric aciduria. No evident clinical phenotypical differences among patients with different pathologic mutations were found when 106 patients with elevated concentrations of 2-hydroxyglutarate in the urine were evaluated.7

Because it is an autosomal recessive disorder, our patient’s parents were counseled regarding the 25% chance that future children will manifest the disorder and the 50% chance that other children will be carriers of the mutation. However, they were not planning to have more children.

1. L-2-Hydroxyglutaric aciduria has a highly characteristic pattern of MRI abnormalities. These include the following:
   1. Symmetrical WM abnormalities with preferential involvement of the subcortical WM with sparing of the internal capsule, corpus callosum, cerebellar WM, and brainstem
   2. Involvement of the dentate nucleus, putamen, caudate, and globus pallidus
   3. Atrophy of the cerebellar vermis and hemispheres may be present

The basal ganglia and dentate nucleus are affected early during the disease with abnormalities of the putamen and caudate nucleus starting at the outer rim and moving inwards.8 These MRI findings can help the clinician differentiate from other cerebral organic acidurias. For example, patients with glutaric aciduria type 1 will have temporal lobe hypoplasia, dilated sylvian fissures and external CSF spaces, and T2 hypointensities.

Organic acidurias can be divided into classical and cerebral groups based on their clinical features.1 Patients with classical organic acidurias usually present with acute metabolic decompensation after a short symptom-free period at birth. In contrast, cerebral organic acidurias such as L-2-hydroxyglutaric aciduria typically present with neurologic symptoms in the absence of severe metabolic derangements. The pattern of presentation of the neurologic symptoms can
also help distinguish between the different cerebral organic acidurias. For example, in glutaric aciduria type I the symptoms occur acutely, while in 1,2-hydroxylglutaric aciduria there is more of an insidious onset with slow progression. However, the neurologic symptoms themselves usually overlap between different conditions and alone would be poor predictors of a specific cerebral organic aciduria. Clinically, most patients with 1,2-hydroxylglutaric aciduria present in childhood with developmental delay usually consisting of mild to moderate psychomotor retardation. Cerebellar ataxia and epilepsy occur in about two-thirds of patients while macrocephaly and extrapyramidal symptoms are present in half. Hypotonia is usually prevalent in the early stages of the disease with spasticity appearing later. Our patient demonstrates many of these characteristic features, including macrocephaly, dysarthria, ataxia, mild hypotonia, and cognitive delay. No epidemiologic studies are yet available to determine incidence, life expectancy, or whether incidence differs by ethnicity. However, disease progression is usually slow, with most patients reaching adulthood.5

Only 2 case reports in the literature document specific therapies producing improvement of neurologic function with decrease in the urinary excretion of 1,2-hydroxylglutaric acid.3,9 Further studies are needed to identify therapeutic strategies that decrease cerebral formation of 1,2-hydroxyl glutaric acid. The improvement in neurologic function following biochemical alteration is encouraging for the future outlook of this rare disease.

AUTHOR CONTRIBUTIONS
Dr. Cachia was responsible for drafting and revising the manuscript for content, including medical writing for content, study concept and design, acquisition and analysis of data, concept, and analysis of data. Dr. Stine was responsible for drafting and revising the manuscript for content, including medical writing for content, analysis and interpretation of data, and study supervision.

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REFERENCES
8. Desai NK, Runge VM, Crisp DE, Crisp MB, Naul LG. Magnetic resonance imaging of the brain in glutaric acidemia type I: a review of the literature and a report of four new cases with attention to the basal ganglia and imaging technique. Invest Radiol 2003;38:489–496.
Clinical Reasoning

Clinical Reasoning focuses on case presentations with the aim of developing clinical reasoning skills among trainees. Appropriate cases for publication would include uncommon presentations of common neurological disorders and also typical presentations of more exotic disorders. The emphasis of the case presentation should be on generating a sound, thorough differential diagnosis; logically arriving at the correct diagnosis; and thoughtfully discussing the teaching-points of the case. Cases discussed in the section should utilize data presented serially in two to four segments that could be opened sequentially by the reader, allowing them to challenge themselves by thinking through the differential diagnosis or treatment options at each step. The manuscript should indicate where each break would occur, with specific questions for the reader to consider as they work their way through the case. The final section should provide the experienced clinician’s discussion (or resident author’s literature review). Ideally the individual sections will also include visually presented data, such as radiology, EEG, EMG, or other studies. See published samples as examples.
Clinical Reasoning:
A 44-year-old woman with headache followed by sudden neurologic decline

SECTION 1
A 44-year-old woman with a history of migraines and idiopathic intracranial hypertension presented to the emergency room with 1 day of headache and nausea. She had been otherwise healthy with no sick contacts. She was afebrile without nuchal rigidity, rash, or cardiac murmur, and her neurologic examination was normal. Migraine therapy was initiated with IV prochlorperazine, ketorolac, and magnesium. Two hours later, she developed fever (101.4°F) and confusion, continually stating, “It hurts,” but unable to answer questions or follow commands despite an otherwise unremarkable examination. Noncontrast head CT demonstrated mastoid sinus opacification, but no abnormalities of her brain parenchyma or ventricular system.

Question for consideration:
1. How should one evaluate and manage the patient?

SECTION 2
The patient’s headache, fever, and confusion raise concern for meningitis or encephalitis, and likely sinusitis on CT implicates a potential source for infection. Antibiotics should be initiated immediately when meningitis is considered likely. Until culture results are obtained, therapy should target the most likely pathogens in a given patient population. Vancomycin and a third-generation cephalosporin (e.g., ceftriaxone) are recommended to treat Streptococcus pneumoniae and Neisseria meningitidis, the 2 most common pathogens in immunocompetent children (older than 1 month) and adults up to age 50. Immuno compromised, infancy, or advanced age warrant ampicillin therapy against Listeria monocytogenes. A third-generation cephalosporin effective against Pseudomonas (i.e., cefepime, ceftazidime) should be considered in patients with penetrating trauma, ventriculoperitoneal shunt, or following neurosurgery. If there is concern for encephalitis, acyclovir should be empirically initiated while awaiting herpes simplex virus PCR. Antibiotics should be administered prior to lumbar puncture (LP), since CSF cultures do not become sterile until 2 hours from antibiotic administration for meningococcus and 6 hours for pneumococcus, and cellular/biochemical changes last 48–68 hours.1

Dexamethasone is recommended in the treatment of adults with meningitis, based on the results of a randomized trial studying 301 patients.2 Patients who received dexamethasone (10 mg every 6 hours for 4 days) beginning 15–20 minutes prior to or with the first dose of antibiotics had a significant decrease in unfavorable outcomes and death. This result was driven by patients with pneumococcal meningitis, with no significant benefit to dexamethasone therapy for other organisms, and greatest benefit seen in moderate to severe cases of meningitis.

In our patient, ceftriaxone, vancomycin, and dexamethasone were initiated. LP revealed opening pressure of 49 cm CSF, protein of 286 mg/dL, glucose less than assay, 117,200 white blood cells (100% polymorphonuclear cells), 30 red blood cells, and moderate Gram-positive cocci in pairs (cultures grew penicillin-sensitive Streptococcus pneumoniae). The patient was admitted to the medical intensive care unit (ICU) where she opened her eyes to voice, tracked, had bilaterally reactive pupils, and moved all 4 extremities equally, but was not following commands. Due to persistent complaints of pain, she received several doses of IV opiates over the 8 succeeding hours. Approximately 12 hours after her initial presentation (6 hours after her LP), her oxygen saturation suddenly fell to 80% and she was found to be apneic.

Question for consideration:
1. What is the differential diagnosis for her sudden respiratory arrest?
SECTION 3
Complications of meningitis that can cause acute deterioration include cerebral edema, hydrocephalus, cerebral infarction, cerebral venous sinus thrombosis, and seizure. The patient received naloxone in the event that recent opiate administration had caused her decline, but she did not improve and was intubated. On examination off sedation, she opened her eyes to voice, tracked, had equal and reactive pupils, full extraocular movements to command with prominent gaze-evoked nystagmus in all directions, corneal reflexes bilaterally, and spontaneous, symmetrical mouth movements. She was unable to protrude her tongue, had no gag reflex, and could not move any extremity spontaneously or to noxious stimuli. She had no spontaneous respirations.

Question for consideration:
1. What is the localization of her examination findings?

SECTION 4
The patient’s ability to follow commands demonstrates preserved function of the cerebral cortex and its projections from the reticular activating system in the midbrain and thalami. Her preserved eye and mouth movements indicate intact brainstem function above the caudal pons. Prominent nystagmus in all directions of gaze indicates vestibulocerebellar dysfunction. Lack of gag, inability to move the tongue, apnea, and flaccid paralysis also suggest dysfunction at the level of the medulla. Head CT revealed no abnormalities. Brain MRI (obtained 12 hours after her acute decline) demonstrated diffusion restriction consistent with acute infarction in the bilateral cerebellar hemispheres as well as the medulla extending into the cervicomedullary junction (figure). CT angiogram obtained after her MRI did not reveal arterial occlusion, dissection, or venous sinus thrombosis. Echocardiogram was normal, with no valvular abnormalities or vegetations.

Question for consideration:
1. What is the cause and management of her condition?

Figure MRI

(A) Axial diffusion-weighted imaging (DWI) and (B) apparent diffusion coefficient (ADC) sequences show infarction of the bilateral cerebellar hemispheres as well as portions of the medulla. (C) Coronal and (D) sagittal postcontrast T1 magnetization-prepared rapid gradient echo (MPRAGE) sequence images show descent of the cerebellar tonsils into the foramen magnum, compressing the brainstem.

GO TO SECTION 5
SECTION 5
The patient likely developed increased intracranial pressure (ICP) causing transtentorial herniation of the cerebellar tonsils. This led to compression of the arterial supply to structures near the foramen magnum, resulting in infarction of her cerebellum and medulla. To relieve her increased ICP and prevent complications from further cerebral edema, she was treated with hyperosmolar agents (hypertonic saline and mannitol), placement of an external ventricular drain (EVD) for CSF diversion, and decompressive suboccipital craniectomy. Despite these measures and the eradication of her infection, there was no improvement in her quadriplegia, anarthria, or ventilator dependence.

DISCUSSION
Brain herniation in acute bacterial meningitis has been described in a number of case reports and series, and has been estimated to occur in 5% of cases.1 Severe inflammation can cause cerebral edema and impairment of CSF flow. The resultant elevated ICP may create a pressure gradient between the skull contents and spinal column. LP may precipitate herniation due to exacerbation of this pressure gradient, though a cause-effect relationship is debated.1,4 In a review of 98 reported cases of herniation in acute bacterial meningitis, 11% of herniation events occurred prior to LP, 38% occurred within 3 hours of LP, and 41% occurred between 4 and 12 hours following LP.1 While imaging findings of midline shift and effacement of the fourth ventricle or cisterns are obvious contraindications to LP, CT is insensitive for predicting elevated ICP in the setting of meningitis, since decreased compliance of inflamed meninges and ventricular walls may counteract the forces of cerebral edema, yielding a falsely reassuring ventricular appearance.1,5

Seizures, focal neurologic deficits, papilledema, and altered consciousness may predict increased ICP in the setting of normal-appearing radiologic images in acute meningitis.1,6 While some experts propose that these clinical signs warrant performance of CT prior to LP,7 others suggest that their presence should lead to deferment of LP.3 The potential diagnostic uncertainty if LP is deferred may be mitigated by laboratory testing such as blood cultures (positive in 40%–50% of patients with meningococcal meningitis and 80%–90% with pneumococcal or Hemophilus meningitis).1 The theoretical risk of inadequately treating an undetermined bacterial pathogen insensitive to typical coverage may be minimal (0.3%) compared to the overall incidence of herniation in meningitis (5%), and the risk of missing alternative diagnoses without LP data could potentially be compensated for by alternative means of data collection (e.g., signs of tuberculosis on imaging, malaria on blood smear, or CSF cultures obtained via EVD, if one is placed for management of elevated ICP).1

Our patient had an initial Glasgow Coma Scale score (GCS) of 13 without focal neurologic deficits or seizures and had a normal head CT, yielding no clear contraindication to LP. Although her fundi were not visualized on presentation, papilledema had been noted during prior evaluation for idiopathic intracranial hypertension, complicating the interpretation of funduscopic in her case. Her opening pressure, however, was 49 cm CSF. In patients with clinical signs concerning for impending herniation (e.g., declining GCS, pupillary dilation, focal examination findings), the need for urgent management of ICP is evident. How should one proceed in a patient such as ours with no clinical or radiographic signs of impending herniation? Her acute change in mental status may have been a clue to intracranial hypertension, though LP is routinely performed in the diagnostic evaluation of altered consciousness. Elevated ICP in acute bacterial meningitis is associated with decreased survival.8 An elevated opening pressure on LP in this setting reflects an acute process, and requires urgent intervention to reduce the risk of brain herniation. In presumed acute bacterial meningitis, if LP reveals an elevated opening pressure, we recommend immediate cessation of CSF removal, treatment with hyperosmolar therapy, consideration of placement of an ICP monitor and CSF diversion, and close monitoring in an ICU. A randomized controlled trial examining use of an osmotic agent (glycerol) in children with meningitis demonstrated a significant decrease in death and severe neurologic sequelae with hyperosmolar therapy.9 Hyperosmolar therapy is considered safe and effective,10 and the risk of complications (e.g., renal failure and volume overload or depletion) is balanced by the potential for prevention or reversal of brain herniation. ICP monitoring allows for tailored hyperosmolar therapy and CSF diversion (if an EVD is used), benefits that may outweigh the risks of the procedure (e.g., intracebral hemorrhage and insertion of a foreign body during active infection) in acute bacterial meningitis with elevated ICP.

AUTHOR CONTRIBUTIONS
Dr. Berkowitz drafted the initial manuscript, revised the manuscript, and was involved in the clinical care of the patient. Dr. Kimchi drafted the initial manuscript, revised the manuscript, and was involved in the clinical care of the patient. Dr. Hwang revised the manuscript and was involved in the clinical care of the patient. Dr. Vasilevicius was involved in the clinical care of the patient. He reports no disclosures. Dr. Henderson revised the manuscript and was involved in the clinical care of the patient. Dr. Foske revised the manuscript and was involved in the clinical care of the patient. Dr. Joseph drafted the initial manuscript, revised the manuscript, and was involved in the clinical care of the patient.

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General Submission Instructions

The Resident and 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 and Fellow Section. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.

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:
Changing practice
Residents’ adoption of the atraumatic lumbar puncture needle

Christie E. Tung, MD

ABSTRACT
Background: The atraumatic needle is recommended over the cutting needle to prevent complications related to lumbar puncture and to reduce costs to the health care system. However, very few practicing neurologists use the atraumatic needle, which in turn limits the teaching of its use to neurology residents. Despite this, neurology residents may be able to adopt the atraumatic needle for lumbar punctures.

Methods: Residents at one neurology residency program were given didactic sessions regarding the atraumatic needle and the opportunity to practice using a lumbar puncture simulator. After the first time a resident performed a lumbar puncture with the atraumatic needle, he or she was asked to complete an electronic survey.

Results: The reported mean number of lumbar punctures performed using the cutting needle prior to the study was 25. Eleven residents (92%) who used the atraumatic needle said they would use it again for future lumbar punctures. The most common reasons cited for wanting to continue to use the atraumatic needle were to prevent post-lumbar puncture headaches, to choose the cost-effective option, and to stay up-to-date with changes in practice.

Conclusion: Neurology residents can successfully adopt the atraumatic needle as standard of care for lumbar punctures. Neurology® 2013;80:e180–e182

GLOSSARY
AAN = American Academy of Neurology; ACGME = Accreditation Council for Graduate Medical Education; PGY = postgraduate year; PLPH = post-lumbar puncture headache.

Lumbar puncture is a routine procedure for neurologists. Post–lumbar puncture headache (PLPH) is a common consequence of lumbar puncture. For every 6 neurology patients undergoing a lumbar puncture with an atraumatic spinal needle instead of a standard cutting needle, one patient will be prevented from having a PLPH.¹ Despite clear evidence that the atraumatic needle effectively prevents PLPH compared to the cutting needle, as well as the recommendation of the American Academy of Neurology (AAN) that the atraumatic needle replace the cutting needle for use in lumbar punctures, few established neurologists have adopted its use.² A survey conducted in 2001 of senior, fellow, and active AAN members in the United States found that only 2% of neurologists use the atraumatic needle. The most common reasons given by neurologists for not using the needle were not having knowledge of atraumatic needles, non-availability of the needles, expense, slow flow, and difficulty of use.³ The results of multiple studies have contradicted criticisms of increased technical difficulty, altered flow dynamics, and increased cost associated with the atraumatic needle. The atraumatic needle was recently shown to be cost-saving compared to the cutting needle. Based on prevention of PLPH alone, the atraumatic needle may save at least $10.4 million per year to the health care system.⁴

Lumbar puncture technique is commonly taught during residency. Residents learn primarily by watching others. Teaching regarding use of the atraumatic needle is significantly limited by the number of neurologists who do not know of or use the atraumatic needle. Despite this, given their relative inexperience compared to practicing neurologists, neurology residents may have

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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.
fewer biases toward using one needle over the other. Residents may be able to easily adopt the atraumatic needle for lumbar punctures.

**METHODS** Adult and child neurology residents (20 total, postgraduate years [PGY] 2–5) at one neurology residency program were strongly encouraged to attend at least one of 2 didactic sessions held by the study author (also a resident) regarding the atraumatic needle. During these hour-long sessions, evidence was presented from previously published studies regarding the atraumatic needle, including decreased risk of PLPH, cost savings, ease of use, and flow dynamics.2–6 Residents were given samples of the atraumatic needle (22-G Sprotte) to compare to the cutting needle (20-G Quincke). Residents also observed a lumbar puncture with the atraumatic needle performed on a lumbar puncture simulator and had the opportunity to practice on the simulator. The study period began after the second didactic session. After the first time a resident performed a lumbar puncture with the atraumatic needle in any clinical setting, he or she was asked to answer a brief electronic survey. The survey was developed from a review of published literature and research questions. The survey consisted of 10 total questions, a mix of Likert, yes/no, and multiple response items. Residents were given 5 days post-lumbar puncture to answer the survey. Residents received weekly e-mail reminders to participate promptly in the survey after performing a lumbar puncture using the atraumatic needle for the first time. Survey responses were collected over a total time frame of 6 months after the atraumatic needle became available at the study site. Survey respondents’ identities were undisclosed to the author and there was no access to information that could allow identification of the respondents.

**RESULTS** At the beginning of the study period, none of the residents had ever used the atraumatic needle. A total of 80% of residents attended at least one didactic session. At the end of the 6-month study period, all of the residents who had the opportunity to perform at least one lumbar puncture (12 out of the 20) had used the atraumatic needle. These 12 residents consisted of 4 PGY-4 level residents, 6 PGY-3 level residents, and 2 PGY-2 level residents. The residents reported having used the cutting needle for prior lumbar punctures anywhere from 8 to 50 times before the study period. The reported mean number of lumbar punctures performed using the cutting needle prior to the study period was 25.

Twenty-five percent of residents who used the atraumatic needle reported that using the introducer that accompanied the needle was "extremely easy" and 60% reported that using the introducer was "very easy." About 80% of residents reported that successfully inserting or positioning the atraumatic needle was at least "just as easy" as inserting the cutting needle. All 10 residents who successfully obtained CSF reported that collecting CSF through the atraumatic needle was at least "just as easy" as collecting CSF through the cutting needle. Of the 2 residents who did not successfully obtain CSF using the atraumatic needle, after switching to the cutting needle one successfully collected CSF and the other did not. When asked why they believed they were not successful using the atraumatic needle, one resident endorsed difficulty with placement or positioning of the needle, one resident endorsed poor patient cooperation with the procedure, and both residents endorsed that the anatomical landmarks on the patients were not easily palpable prior to the procedure. One of the 2 residents who did not initially successfully use the atraumatic needle was successful using the atraumatic needle during subsequent lumbar punctures. Eleven residents (92%) who used the atraumatic needle said they would use it again for future lumbar punctures. The most common reasons cited for wanting to continue to use the atraumatic needle were to prevent PLPH, to choose the cost-effective option, and to stay up-to-date with changes in practice.

**DISCUSSION** The traditional teaching paradigm in medicine is from the top down, i.e., knowledge from attending physicians is handed down to residents. The limited number of physicians who use the atraumatic needle is an obstacle to its widespread implementation. Few examples exist in the literature of practicing neurologists attempting to introduce the atraumatic needle into routine practice. At one institution, atraumatic needles were introduced and made available to staff conducting lumbar punctures. Over the course of 1 year, atraumatic needle use increased from 0% to 37% of lumbar punctures.7 In our study of residents, over the course of 6 months, use of the atraumatic needle increased from 0% to 60%. A collaborative effort between attending physicians and residents to learn how to use the atraumatic needle would likely benefit all and increase implementation within the specialty.

Our study utilized a lumbar puncture simulator for teaching lumbar puncture technique. In regards to teaching procedural technique, the status quo of top-down teaching by attending physicians and observation-based learning by residents may lead to inferior skill acquisition compared to simulation-based learning. This was recently demonstrated in the acquisition of lumbar puncture technique in particular.7 By providing learners with a safe environment to practice procedural skills and receive feedback, simulation technology increases skill acquisition.8 The incorporation of simulation-based training in teaching lumbar puncture technique may further facilitate implementation of the atraumatic needle.

Residents in this study indicated they would continue to use the atraumatic needle for multiple reasons, including choosing the cost-effective option. Teaching physicians at some academic centers may not prioritize the teaching of cost-effective models of care due to the belief that resident learning requires some tolerance of inefficiency. Also, teaching of cost-
effective care models may be perceived as conflicting with centers' research and education missions. However, these missions are at odds with values defined by the Accreditation Council for Graduate Medical Education (ACGME). The ACGME has named 6 Core Competencies on which residents are regularly evaluated and are expected to achieve to complete residency. Providing cost-effective care falls under the umbrellas of 2 of the core competencies. Competency in “systems-based practice” is defined as an awareness of and responsiveness to the larger context of the health care system and the ability to effectively call on system resources to provide care. At the heart of this competency is a fundamental understanding of how patient care relates to the overall health care system. Second, the competency of “practice-based learning and improvement” evaluates residents’ use of evidence-based medicine and best-available evidence. The incorporation of cost-effective care education and cost-saving technologies such as the atraumatic needle into residency educational programs would allow for compliance with and mastery of both core competencies.

This study was limited by the relatively small number of survey participants at only one residency program. The results of this study are based on self-reports from participants, which allows for possible reporting bias. Future studies involving a larger sample population would be helpful in clarifying whether these results can be generalized to a larger population.

Neurology residents can successfully adopt the atraumatic needle as standard of care for lumbar punctures. This study demonstrates residents’ preference for the atraumatic needle over the cutting needle in order to prevent PLPH, to choose the cost-effective option, and to stay up-to-date with changes in practice. The limited experience of teaching neurologists regarding the atraumatic needle should not prevent neurology residents from its use. A change in practice among all neurologists may occur if neurology residents continue to learn to use the atraumatic needle.

STUDY FUNDING
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DISCLOSURE
The author reports no disclosures. 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 and Fellow Section Editor before submission to inquire about the need for an article on a particular topic.
Global health is the study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide. In contrast to the public health concerns of a particular country or region, global health looks at populations irrespective of borders. One of the key elements in advancing the field of global health was the establishment of the WHO in 1948. Since its inception, the WHO has helped coordinate global efforts toward eradicating diseases such as smallpox and polio as well as elimination of onchocerciasis. It now assumes responsibility for the International Classification of Diseases. More recently, the field of global health has received considerable attention from world leaders, philanthropists, and academics. In 2009, President Obama introduced his Global Health Initiative that proposed spending $63 billion over 6 years to support global health programs specifically targeting areas such as HIV/AIDS, malaria, tuberculosis, nutrition, and reproductive health. On his first day of work as NIH Director, Francis Collins announced global health as one of his 5 themes of “exceptional opportunity” that would receive special priority during his tenure. The Fogarty International Center is a branch of the NIH that helps to support global health research for US and foreign researchers, often in resource-limited settings. The research initiatives encompass a diverse range of disciplines within the field of medicine.

NEUROLOGY AND GLOBAL HEALTH There is a common misconception, even among those in the field, that neurology is too specialized for global health and that the most pressing issues are best addressed through more general disciplines such as internal medicine or pediatrics. However, according to the WHO, neurologic disorders account for 11% of all of the world’s premature deaths and years lived with disability. Stroke accounts for approximately 10% of deaths worldwide with 85% of stroke occurring in low-income and middle-income countries. Though the field of neurology as it applies to global health in many ways is still in its nascent stages, there is a successful history of coordinated global efforts in addressing neurologic diseases. The directed study of families from Ohio and the shores of Lake Maracaibo, Venezuela, were central to the mapping of the Huntington disease gene. The discovery of human T-lymphotropic virus 1 (HTLV-1) in the United States allowed researchers to prove that tropical spastic paraparesis in the Caribbean and in Japan were the same disease, now called HTLV-1-associated myelopathy.

The need to attract neurologists into the field of global health is further highlighted by the burden of neurologic diseases and the relative lack of neurologic expertise particularly in resource-limited settings. Two-thirds of the neurologic disease burden occurs in the developing world, including 80% of epilepsy cases. In one survey, 35 of 50 African nations (70%) had 4 or fewer neurologists in the country, with 12 nations completely lacking neurologists. In these settings, the presence of a neurologist is a relatively recent occurrence and most generalists have received their training in almost total absence of neurologic specialty skills. As a result, many neurologic conditions are unrecognized and remain untreated. Furthermore, cognitive dysfunction associated with neurologic diseases undermines compliance with treatment of common medical conditions. Neurologists engaging in global health activities can help build local capacity through training and research so that there is enduring expertise within countries. In addition, neurology global health specialists can advise policymakers on issues related to treatment gaps, drug costs, and public health campaigns as they apply to neurologic illness.

GETTING INVOLVED There are varying levels of engagement for a neurologist to become involved in global health activities. At a training level, a number of neurology residency training programs around
the United States have developed relationships with institutions in resource-limited settings where trainees can perform clinical electives. These electives provide valuable opportunities for trainees to gain exposure to uncommon diseases as well as a chance to formulate research questions applicable to a specific setting. In addition, the World Federation of Neurology (WFN) formed the International Working Group of Young Neurologists and Trainees to support international training exchange. Neurologists further along in their careers can perform short stints as visiting professors in underserved regions. The WFN Visiting Professors Program in Zambia has sponsored a number of academic neurologists from all over the world to spend a month in Zambia to provide clinical work and teaching to trainees in Zambia. The Movement Disorder Society has a similar program in under-represented countries. There are global health opportunities within medical education. In recognition of the heterogeneity in neurologic training across Europe, the European Association of Young Neurologists and Trainees is working toward harmonizing training across the region. Another potential area of engagement is at the level of a neurologic society. A successful example of this is the Nigeria Florida Neuroscience Partnership with its goal to improve the state of neurologic care and education in Nigeria. The American Academy of Neurology has recently recognized the increasing importance of global health as it applies to neurology with the formation of a Global Health Section (http://www.aan.com/go/about/sections/global).

CAREER PROSPECTS The possibility also exists to have a career that is fully dedicated to neurology global health activities. There are numerous funding opportunities available to neurologists who are interested in conducting global health research (table e-1 on the Neurology® Web site at www.neurology.org). The success from small research projects can often lead to more substantial funding toward a more comprehensive study. There are several models for an academic neurologist from the United States choosing to focus on global health. An individual can be based full-time at a foreign institution through a funded research project while maintaining an academic affiliation with a medical center in the United States. The advantage to living overseas full-time is that neurologists can embed themselves into a country, helping to improve neurologic services and education from the ground. Another model is spending a significant portion of the year outside the country, engaging in research activities with the help of in-country collaborators. This is most easily done when a reliable research team or local partners are present to carry out activities when the researcher returns home. A final model would be a neurologist based in the United States who makes periodic visits to a particular site in order to supervise research or clinical care. There are a number of academic neurologists from the United States who follow the models outlined above. An alternative approach would be to pursue a position through a public agency such as the NIH, Centers for Disease Control and Prevention, or WHO, all of which have global health programs that include neurologic illness.

DISCUSSION The need for neurology global health specialists continues to grow as the world becomes increasingly interconnected and various neurologic illnesses, once confined to specific regions, now appear in novel settings. With more neurologists participating in global health activities, the specialty will become more easily accessible to those who have an interest in the field but are unclear how to become involved. An increase in funding opportunities would also entice more neurologists into the specialty and help support it as a legitimate career path. It is imperative to bring global health further into the consciousness of the neurology community in order to achieve the specialty's ultimate goal: equity in neurologic care throughout the world.

AUTHOR CONTRIBUTIONS O. Siddiqi contributed to the study concept and design of the manuscript. I. Koranik contributed a critical revision of the manuscript for important intellectual content. M. Atadzhyan contributed a critical revision of the manuscript for important intellectual content. G. Birbeck contributed a critical revision of the manuscript for important intellectual content.

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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 3-year residency cycle. Submissions should be timely and are requested no longer than 4 weeks following the original e-Publication date of the subject article. These Journal Club critiques, written by neurology residents and fellows with faculty supervision, should follow a specific outline and contain subtitles for background and significance, hypothesis and design, methods, results, and interpretation. Rather than a critical correspondence or editorial, this feature will highlight methods for the critical appraisal of medical literature. This online feature could be used as an adjunct to traditional institutional journal clubs and promote discussion among neurologists, including trainees and those in practice.
Journal Club:
Randomized phase III study 306
Adjunctive perampanel for refractory partial-onset seizures

BACKGROUND AND SIGNIFICANCE A working understanding of antiepileptic drug development, critical appraisal of drug trial design, and interpretation of study results are fundamental for the neurologist and epileptologist, to incorporate newer anticonvulsant medications into clinical practice. In this Journal Club, we evaluate a phase III study by Krauss et al.,
that demonstrates efficacy and safety of adjunctive perampanel for refractory partial-onset seizures.

Perampanel is a highly selective, noncompetitive α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)-type glutamate receptor antagonist. AMPA receptors mediate the excitatory actions of glutamate and are essential in the generation and spread of epileptic activity. Development of other related glutamate receptor antagonists as potential anticonvulsants, including N-methyl-D-aspartic acid receptor antagonists and other AMPA receptor antagonists, has been disappointing. However, interest in perampanel has escalated because it has been shown to reduce seizure activity in several animal models of epilepsy, and preliminary safety and tolerability of oral perampanel (2–12 mg/d) have been demonstrated in 2 phase II dose-escalation, placebo-controlled studies. This study adds Class I evidence of the efficacy and safety of adjunctive perampanel at 4 and 8 mg/d doses in reducing partial onset seizures. Such controlled phase III trials are required, in part, by regulatory agencies before consideration for approved clinical use.

HYPOTHESIS AND DESIGN The essential question being investigated is whether perampanel, a drug with a unique mechanism of action, is a potentially valuable medication for the treatment of epilepsy. This is a relevant question, because despite the near yearly introduction of new antiepileptic drugs, more than a third of patients with epilepsy continue to be medication-refractory.

Specifically, the investigators focused on obtaining data on the efficacy and safety of adjunctive perampanel within their study population. Efficacy refers to measured improvement within the narrow predefined boundaries of the clinical trial. In this case, the boundaries defined a specific patient population being treated with a preset dosing of perampanel as those 12 years of age and older with medication-refractory partial onset seizures, and excluding patients according to predetermined listed criteria. Patients were followed for 19 weeks in the double-blind treatment phase. Doses and titration were defined to evaluate the dose response.

The design set forth by the investigators optimized its feasibility for completion of the study. The study recruited adults and children 12 years and older with medication-refractory partial seizures. End points for defining efficacy were specified to be seizure count reduction and responder rate (percentage of patients who experienced a 50% or greater reduction in seizure frequency) in order to reduce the sample size needed to demonstrate significant treatment differences. If an end point of seizure freedom was chosen, this would have required a larger study population, because seizure freedom would be expected to occur in only a small subset of patients already proven to be medication-refractory.

METHODS Patients aged 12 years and older from 116 centers in 24 countries with refractory simple partial or complex partial seizures, with or without secondary generalization, were enrolled. Subjects were taking 1 to 3 antiepileptic drugs and were randomized if they had at least 5 partial seizures in the 6-week baseline period. This was followed by a 19-week treatment phase (6-week titration and 13-week maintenance period) with either adjunctive placebo or perampanel in doses of 2, 4, or 8 mg/d. Higher dose treatment groups (4 and 8 mg/d) were titrated at 2 mg/d each week to the respective goal doses.

The primary end points were the percentage change in seizure frequency per 28 days based on seizure counts from patient diaries and responder rate, defined as the fraction of patients with a 50% or more reduction in seizure frequency. Percentage change in frequency of seizures and dose-response analysis of percentage change in seizures were used as secondary end points.

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The views expressed in this article are those of the author(s) and do not reflect the official policy or position of the United States Air Force, Department of Defense, or the U.S. Government.
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Safety was assessed using proactive reporting of adverse effects using questionnaires, laboratory results, and physical examination.

RESULTS Of the 706 patients appropriately randomized, 623 patients completed the study, and 83 did not, including 32 because of adverse events. The median seizure frequency during the 6-week baseline period was 9.3 to 10.9 seizures per 28 days.

The median percentage change in seizure frequency was $-10.7\%$ for placebo, $-13.6\%$ for 2 mg/d, $-23.3\%$ for 4 mg/d, and $-30.8\%$ for 8 mg/d, with statistically significant $p$ values for 4 mg/d ($p = 0.003$) and 8 mg/d ($p < 0.001$) groups compared with placebo by rank-transformed analysis of covariance. Because of the skewed distribution of seizure frequency, data at baseline and seizure per 28 days during treatment were rank transformed before regression analysis. The 50\% responder rate was 17.9\% for placebo group and 20.6\%, 28.5\%, and 34.9\% for the 2, 4, and 8 mg/d perampanel groups, respectively. The 4 mg/d ($p = 0.013$) and 8 mg/d ($p < 0.001$) groups were statistically different from the placebo group. Seizure freedom rates were 1.2\% for placebo, and 1.9\%, 4.4\%, and 4.8\% for the 2, 4-, and 8-mg perampanel groups.

Dizziness, fatigue, gait disturbance, and somnolence were the most frequently reported side effects, which were mostly mild or moderate, with some rates twice as high in perampanel groups compared with placebo. A dose-related increase in side effects was seen in the treatment groups. The rates reported for dizziness were 9.7\% in placebo and 10.0\%, 16.3\%, and 26.6\% in 2-, 4-, and 8-mg perampanel groups, respectively. Worsening seizures (>/=50\% increase from baseline) were reported in 15\%, 11\%, 8\%, and 8\% of patients treated with placebo, 2, 4, and 8 mg of perampanel, respectively. Side effects leading to discontinuation from the study (dizziness, convulsion, fatigue, and vertigo) occurred in 3.8\%, 6.7\%, 2.9\%, and 7.1\% with placebo, 2, 4, and 8 mg of perampanel, respectively. No deaths were reported and seizures were the only serious side effect reported in more than 1 group (5 cases in placebo and 2 cases in the 2 mg/d group). No significant changes in laboratory values between groups, vital signs, or EKG parameters were reported.

INTERPRETATION The strength of this study is that it is a randomized, placebo-controlled, double-blinded study. This is the most rigorous way to obtain reproducible data that are both valid and precise. The study was able to generate statistically significant results. There was a linear dose-response relationship with superiority of the test agent compared with placebo. The efficacy and tolerability profile were similar to trial results of newer antiepileptic drugs already in use.

The demonstration of efficacy within a clinical trial does not always translate into clinical effectiveness. Patient populations selected for clinical trials differ from the general patient population, thus results may not always be generalized into clinical practice. In addition, if enhanced clinical efficacy incurs intolerable side effects, this will also diminish the clinical effectiveness. Finally, the 19-week length of the clinical trial demonstrated early efficacy, but it does not offer evidence regarding the long-term durability of the drug's benefit.

The weaknesses of this study are inherent to clinical trials studying the treatment of epilepsy. This includes restrictions to a specific population, dosing regimen, and follow-up duration. In particular, for practical and logistical reasons, children were excluded, leaving clinicians again in the position of extrapolating information from a study to a unique and understudied population. In addition, the results are dependent on patient self-reporting using seizure diaries, which are subject to individual variability in complete and accurate reporting.

The study was not powered to detect rare or serious side effects such as Stevens-Johnson syndrome, aplastic anemia, or liver failure, that occur with other anticonvulsant medications. Because adverse events occurred in a dose-dependent manner, it is possible that blindness was compromised. In fact, this is a recurrent issue in anticonvulsant drug trials that has been under-recognized. Finally, it should be noted that the lead author is a consultant for Eisai Inc. However, knowledgeable investigators are often recruited to participate in study design and conduct, and therefore develop consulting relationships with sponsors of clinical trials.

The authors conclude that the utility of perampanel, at a minimal effective dose of 4 mg, as an adjunctive treatment of uncontrolled partial-onset seizures, is promising, and this is supported by the results of the study. Translation of its use into clinical practice will depend partly on logistical issues—whether further studies can validate these published results. Assessment of clinical effectiveness will also be a key factor. Further research, including prospective, open-label studies and retrospective studies, with additional experience in clinical practice, will reveal the usefulness of perampanel over time. The long-term efficacy and the possible emergence of adverse events not seen during the study period are also important data that will contribute to its use in clinical practice.

In conclusion, the results of this study demonstrating efficacy and safety are a first step to determining whether perampanel will be a valuable adjunctive medication in the clinical care of patients with epilepsy. Perampanel seems to possess properties that are desired in the ideal anticonvulsant medication, including efficacy, modest side effects, and long half-life allowing once a day dosing. The continued
critical appraisal of this study and those studies to follow will allow clinicians to continue to make scientific and practical decisions in clinical practice.

STUDY FUNDING
No targeted funding reported.

DISCLOSURE

REFERENCES
Media and Book Reviews

The Neurology offices frequently receive newly published books, and residents and fellows are invited to review these. Reviewers will be allowed to keep the books. Reviews should be 250-500 words, and include the strengths and weaknesses of books for a trainee audience. Interested individuals should contact the journal (smorianty@neurology.org) for available books to review. We also welcome reviews of online, electronic, and other educational materials, and interested individuals should contact the journal to discuss their ideas.
Media and Book Reviews

UpToDate

*edited by Denise S. Basow, UpToDate, 2013, $499/year ($199/year for trainees)*

In a technological era dominated by a constant barrage of medical and nonmedical information, a challenge for the clinical neurologist and trainee is maintaining quick and efficient access to high-yield, clinically relevant information.

UpToDate is a Web-based application owned by Wolters Kluwer Health that provides access to articles and reviews of over 9,500 topics in 20 clinical specialties. The application is maintained by an editorial board of approximately 5,100 authors, editors, and peer reviewers. UpToDate is commonly used by medical trainees and has over 600,000 clinician users in approximately 149 countries via both Web-based and smart device products. Anecdotal reports and over 30 published articles highlight the ease of querying the database, clinical relevance of the topics, and its ability to enhance medical education and patient care.

UpToDate is accredited by the Accreditation Council for Continuing Medical Education, allowing subscribers the ability to earn CME credit by providing logged hours and a description of the application of one’s findings to clinical practice. New features include a graphics search function, which provides an opportunity to query over 23,000 figures, tables, illustrations, diagrams, and videos. A new Webinar series offers bimonthly video sessions. A “What’s new” section highlights the most important recent updates organized by specialty.

For the neurologist, UpToDate provides an efficient method for querying topics in clinical neurology that fall under several broad categories: 1) diagnostic reviews, which provide information on epidemiologic characteristics, clinical presentations, and diagnostic testing; 2) therapeutic reviews, which provide information on therapeutic approaches and prognosis; 3) medication reviews, which provide indications, dosage, side effects, and other pharmacologic information; and 4) patient handout and other information. The reviews are written in narrative form and are divided into relevant clinical categories. Discussions are heavily evidence-based with embedded citations that provide quick links to the corresponding primary literature. Editors-in-chief of the Neurology section include Dr. Michael Aminoff, Dr. Timothy Pedley, and Dr. Jerome Posner.

Several minor limitations exist. Though pathophysiological mechanisms are reviewed in some articles, they are not the primary focus of most reviews. While easily searchable by disease type, information is organized in the aforementioned categories and does not facilitate querying for specific data, statistics, or questions that fall outside the topic headings above. Pharmacologic reviews are of limited utility, mainly providing a means of referencing Food and Drug Administration–approved dosing regimens and pharmacokinetic/pharmacodynamic information. Medication side effects, specific drug–drug interactions, and other information are often more effectively displayed or searchable in other drug-specific applications. While links to full-text articles are available through the application, journal subscription is required to view the entire article and is not included with the UpToDate subscription. This can substantially limit the ability to access primary literature for individual users.

UpToDate is by far one of the most comprehensive, efficient, and effective means of searching for clinically meaningful information on neurologic diseases. This resource provides an invaluable tool to medical students, residents, and practicing physicians at all levels of training.

Reviewed by Roy E. Strowd, MD

Disclosure: Dr. Strowd serves on the editorial team of the Media and Book Reviews of Neurology®. Go to Neurology.org for full disclosures.

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Note to Book Publishers: *Neurology®* provides reviews of books of interest to the clinical neurologist. Please send any books for possible review in the journal to: Robert A. Gross, MD, PhD, FAAN, Editor-in-Chief, Neurology, 201Chicago Avenue, Minneapolis, MN 55415. Inquiries can be directed to: Journal@neurology.org. Please note that not all books received are chosen for review. We do not return books.
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 1-3 questions. Responses are compiled and then published with the full case.
Mystery Case: An unexpected complication of IV thrombolysis for acute ischemic stroke

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A 46-year-old man with psoriasis and morbid obesity developed acute aphasia and right hemiplegia. As a result of his weakness, he had fallen and struck his right eye on a desk. His presenting examination demonstrated right periorbital ecchymosis without accompanying ptosis, expressive aphasia, left gaze deviation with corresponding hemianopsia, and dense right hemiplegia, summarizing an NIH Stroke Scale score of 13.

Questions for consideration:
1. What is the finding(s) on these noncontrast CT images?
2. Should this patient be treated with IV tissue plasminogen activator (tPA)?

The patient was noted to have a hyperdense abnormality within the proximal left middle cerebral artery on initial noncontrast imaging concerning for acute thrombosis (figure, A). He received IV tPA within 2 hours from symptom onset, and noticed significant neurologic improvement within 20 minutes of initiation of therapy.

Approximately 45 minutes after initiation of IV recombinant tPA, the patient developed increasing monocular blindness and complete closure of the right eye from rapidly progressive periorbital edema and ecchymosis. Re-examination of cranial imaging at presentation and following IV thrombolysis confirmed an enlarging retro-orbital hematoma (figure, B and C). An
emergent lateral canthotomy was performed to de-
compress the optic nerve and within 3 days of orbital
decompression and ischemic stroke treatment, he had
near complete visual and neurologic recovery. Follow-
up cranial and orbital imaging performed 24 hours
after canthotomy demonstrated resolution of the retro-
orbital hematoma (figure, D).

The small retro-orbital hematoma present on the ini-
tial imaging had been overlooked during the screening
and decision-making process to administer thrombolytic
therapy. Although the patient recovered without signif-
ican tuminal cerebral or visual impairment as a result of im-
mediate intervention, it is unclear whether IV recombinant
tPA should be withheld in this context. IV thrombolysis
for ischemic stroke has been performed after vitrectomy
without complication,2 but the presence of intraocular
hemorrhage has led to withholding treatment in other
cases.2

IV tPA has consistently been shown to be safe and
efficacious following ischemic stroke.3 However, thrombo-
lytic treatment should proceed with caution even in
the setting of minor trauma, and this case highlights the
importance of careful inspection and vigilance for unan-
ticipated complications.

AUTHOR CONTRIBUTIONS
Dr. Sheh and Dr. Yee were involved in the care of the patient, study
design, data analysis, and preparation of the manuscript.

STUDY FUNDING
No targeted funding reported.

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

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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 train-
ees. 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 Neu-
rology Consortium of Neurology Residents and Fellows
and through social media. All of the responses that
we received came from individuals rather than groups.
Eighty-seven percent of respondents correctly identified
the hyperdense left middle cerebral artery sign on the
patient’s CT scan, and 33% of respondents identified
the right retro-orbital hematoma. Regarding manage-
ment, 77% of respondents stated that the patient should
receive IV tPA, while the other 23% stated that IV tPA
should be withheld because of the hematoma. The most
complete answer came from Dr. Anil Neelakantan who
recognized that IV tPA could lead to expansion of the
retro-orbital hematoma and compression of the optic
nerve, both of which occurred in this case. Fortunately,
the patient had a near-complete recovery of vision after
an emergent canthotomy.

As the authors have acknowledged in their case
report, the appropriate treatment decision in this sit-
uation is not clear-cut. Nevertheless, it is important to
carefully review neuroimaging in the setting of stroke
following head trauma so that hemorrhagic complica-
tions such as the one in this case can be anticipated.

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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 and Fellow Section Editor before submission to inquire about the interest in specific topics.
Opinion & Special Articles: The lost resident
Why resident physicians still need mentoring

ABSTRACT
Mentoring is deeply rooted in medical practice. More than just a role model, a mentor is invested in the development of the mentee, providing personal and professional support, guidance, and the means for advancement. Mentoring is vital at all levels of medical training and plays an important role in the development of academicians. Increasing clinical demands, the competitive research environment, numerous administrative pressures, and the relative undervaluing of mentoring for faculty promotion have created challenges to resident mentoring. A greater emphasis on promoting mentoring opportunities for residents is needed at many levels. Neurology® 2013;80:e244-e246

Mentoring in medicine has long been a recognized factor in promoting and developing the future of the profession. It is being increasingly recognized as a substantial component of recruitment and retention at all levels of academic medicine. The concept of mentorship has evolved over the years, with a recent report estimating at least 20 definitions in the literature. As opposed to a role model, a mentor is a voluntary and active participant in the personal and professional development of the mentee, offering knowledge, experience, guidance, support, and opportunity for advancement. In the literature, the duality of this relationship has been emphasized and the importance of a nonhierarchical but intimate partnership with both parties receiving gain has been highlighted.

Mentorship literature has traditionally focused on the importance of mentors at the medical student and faculty–junior faculty level. Mentors have been described as a critical ingredient for successful academic careers for faculty. Studies have demonstrated impacts on knowledge acquisition, improved clinical skills, enhanced efficiency, increased research interest, productivity, and improved job satisfaction. The presence of a mentor is highly predictive of a young academic investigator’s attainment of higher levels of career development as measured by publications, grants, leadership, academic rank, income, and job satisfaction. Mentorship can also significantly influence faculty advancement, retention, and promotion.

For medical students, mentoring has also been shown to directly affect academic performance, choice of specialty, interest in research, and pursuit of an academic career. In a survey of new general surgery residents, nearly 50% of residents indicated that mentoring in medical school played a primary role in the decision to pursue a surgical career. The Resident and Associated Society of the American College of Surgeons even correlated the reduction in medical student interest in general surgery to the decline in surgeon–student relationships and recent limitations on direct exposure to mentoring opportunities.

The importance of mentoring to residents has been underemphasized in the literature. In a comprehensive review of mentoring across stages of training, only 4 of the 39 articles related to mentoring at the resident level. Anecdotal evidence indicates that residents seek out mentors in unstructured environments; however, numerous barriers exist, including time constraints, limited resources, insufficient academic recognition for mentors, and a lack of adequate mentor training. Furthermore, in an era where many of the brightest physicians are choosing private practice over academia, a more formalized method for encouraging mentorship may be helpful in retaining some trainees.

Mentoring is deeply rooted in neurology. Even as far back as the 19th century, strong mentoring lineages exist: Guillaume Duchenne de Boulogne (1806–1875) trained Jean-Martin Charcot (1825–1893), who later trained Joseph Babinski (1857–1923). Despite this rich history, a PubMed search of MeSH items “mentor” and “neurology” yields only 14 publications, 12 of which are historical accounts of influential neurologists. Of the 2 articles that review mentoring specifically, the first article describes the Educational Pipeline Program at the University of Pennsylvania, which is a fascinating program designed to bring...
neurology residents, medical students, and undergraduates together with local high school students to teach, learn, and help foster early interest in neurology and the medical sciences. The second is an editorial reviewing the impact of one neurologist's own personal mentor. A third article, not identified by this search, reviews the role of mentoring in sparking interest in pediatric neurology. In this questionnaire-based study, responders identified having a mentor as one of the most influential components that contributed to choosing a career in child neurology.

While it is clear that resident mentoring does occur and may promote early career preparation for some, other residents struggle to find these opportunities, as particularly evidenced in investigation into interns, minorities, and women. Nevertheless, mentoring remains one of the most influential factors in the decision for residents to pursue academic medicine, and structured mentoring at the resident level remains vitally important, particularly for these groups. Some have raised concern about the future of academic medicine, particularly as it relates to declining interest in research, increasing financial dis-incentives, and continued issues for career progression among women. Residents are the future of academic medicine, and while mentors, advisors, and role models can be helpful for those residents pursuing private practice, mentors are vitally important for encouraging interest in academia, providing resources for productive research, advocating for minorities and women, and retaining the future of the field.

How can neurology programs begin to promote more resident mentoring? First and foremost, institutional buy-in is paramount. Anthony DeMaria, editor of the Journal of the American College of Cardiology, recently lamented the under-recognition of academic mentors and called for mentoring roles to be more highly regarded in academia. These same pressures abound in neurology, where limited salary support for teaching and mentoring, increasing demands for productivity, and the challenges of incorporating mentoring into promotional considerations have squeezed mentors out of the equation. A shift in priority will begin when a stronger emphasis is placed on training and developing faculty mentors. In this process, mentors must be clearly differentiated from advisors and role models. A mentor will offer knowledge and experience, guide the mentee in academic pursuits, provide opportunity for advancement and career development, and take an active role in the personal and professional life of the mentee. Institutions can show support through recognizing mentors at award selections and presentations, and when screening potential recruits. Resident teaching awards for praised faculty are not uncommon in many neurology departments. A resident mentor award may be an example of a small means of appreciating and encouraging such a mentoring presence. Most importantly, dedication to and success in mentoring needs to be a promotional consideration for faculty.

One of the biggest challenges for resident mentees is finding a mentor. Systematic reviews of faculty have found that fewer than 20% of faculty members had a mentor and that women perceived that they had more difficulty finding mentors. While most believe that mentors should be self-identified and not formally assigned, many have indicated that guidance in finding a mentor would be helpful. A recent report by the Neurology Academy Advisory Committee described the use of an advisory committee or team of individuals as an adjunct to the individual mentorship paradigm.

At our institution, a combined approach has been developed such that young residents are advised by a Resident Advisory Committee comprised of a team of revered senior faculty members from a variety of specialties within neurology including neuropsychology, pediatric neurology, and others. This team of individuals not only provides the supportive framework necessary for transitioning to residency, but also is able to shepherd residents through the necessary steps for self-selection of a faculty mentor. We have considered additional or adjunctive approaches including involvement of a senior-level resident into this advisory structure to provide further resident perspective and facilitate a vertical continuum of potential advisors out of which mentoring relationships at multiple levels become possible. Our anecdotal experience is extremely positive in terms of feedback, research participation, and future career choices. We have observed tangible benefits for residents pursuing both academic and private practice careers.

CONCLUSION Mentoring is deeply rooted in neurology but increasing clinical, research, and administrative demands as well as relative undervaluing of mentoring by academic institutions challenge this tradition. Mentors should focus on helping their mentees with obtaining resources, personal and professional development, and being an advocate for academic medicine. Mentees should focus on identifying an appropriate mentor or mentors. Residency programs should more formally structure a process necessary to achieve this goal and medical schools should recognize the value of mentoring in faculty promotion proceedings.

AUTHOR CONTRIBUTIONS
Dr. Strode: drafting/revising the manuscript, study concept and design. Dr. Reynolds: drafting/revising the manuscript, mentoring the corresponding author.

STUDY FUNDING
No targeted funding reported.

DISCLOSURE
Dr. Strode serves on the editorial team of the Resident & Fellow Section of Neurology®. Dr. Reynolds reports no disclosures. Go to Neurology.org for full disclosures.
RESIDENT & FELLOW SECTION: CALL FOR AUTHORS INITIATIVE

Residents and Fellows (R&F) can visit the Call for Authors page and sign up to ‘check out’ a topic: http://neurology.org/site/feature/callfortopic.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 6 weeks of commitment.

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: Ictal syncope in a patient with temporal lobe epilepsy

PEARLS

- Ictal cardiac arrhythmias are common autonomic features of focal epilepsy.
- Ictal sinus tachycardia and bradycardia are the most common arrhythmias, with ictal asystole occurring infrequently.
- Ictal syncope is a late clinical manifestation of ictal asystole and may contribute to sudden unexplained death in epilepsy.

OY-STERS

- Ictal asystole and ensuing syncope can be easily misdiagnosed as vasovagal syncope, but can be correctly identified by video-EEG. There should be a high degree of suspicion in patients with epilepsy despite the lack of coexisting typical seizure semiology.

CASE REPORT We present a case of an 18-year-old Caucasian woman of normal development with a history of complex partial seizures and new-onset recurrent syncopal episodes. Her typical seizures started at 14 years of age and consisted of staring spells with motor automatisms involving both upper extremities. Her seizures were well-controlled on oxcarbazepine, and she was seizure-free for more than 2 years. MRI revealed a right temporal-occipital cavernous angioma. She presented acutely with recurrent syncopal episodes over the span of 2 weeks with increasing frequency up to multiple times per week. Witnessed episodes were described as sudden loss of consciousness with subsequent falling, without any preceding, concomitant, or postevent seizure-like activity. She denied prodromal symptoms such as palpitations, headache, sweating, abdominal discomfort, nausea, or vomiting. She denied any aura and was completely amnesic for the event. She had a quick return to baseline with brief confusion lasting only a few seconds. The events lasted less than a minute. Initial cardiac workup including EKG, 2D echo, and cardiac biomarkers revealed normal cardiac function. The cavernous angioma was unchanged on repeat imaging. General physical examination including orthostatic blood pressure was normal. Neurologic examination was also normal. She was admitted to our epilepsy monitoring unit where a typical syncopal episode was captured on the day of admission.

Video-EEG captured her typical syncopal event and was consistent with the diagnosis of ictal syncope (IS). A right posterior temporal electrographic seizure was captured. The ictal activity induced cardiac bradycardia and 16 seconds of cardiac asystole ensued with resultant loss of consciousness and tone. This loss of consciousness lasted for 30 seconds and was followed by a quick return to baseline mental status. The figure illustrates the electrographic and EKG findings with clinical commentary.

A cardiac pacemaker was successfully placed in our patient and she was continued on one antiepileptic drug. Oxcabarazpine was switched to levetiracetam to minimize potential risk of arrhythmias. She remained seizure-free and syncope-free. The patient subsequently had excision of the cavernoma and is currently scheduled to have the pacemaker removed as well.

DISCUSSION Paroxysmal loss of consciousness commonly results in neurologic consultation to aid in the differentiation between seizure and syncope. To make this distinction, a thorough history, physical examination, and, most importantly, a reliable witness account are often required in conjunction with a well-thought-out diagnostic workup. Typically, syncope is associated with a prodromal phase of autonomic dysfunction, manifested as lightheadedness, palpitations, chest pain, and sweating. At times, there are triggers of micturition, cough, or postural change. Seizures can be associated with brief abdominal or psychic aura, staring, automatisms, forced deviation of the head, convulsions, and postevent confusion. Myoclonus or convulsion, however, can occur after an episode of syncope, referred to as convulsive syncope. IS, on the other hand, results from seizure activity inducing autonomic dysregulation of the heart in the form of ictal asystole (IA).

Cardiac autonomic dysregulation and arrhythmias, most frequently tachycardia, are common during epileptic seizures. However, ictal bradycardia
Panels B to F are contiguous. (A) Twenty seconds prior to seizure onset, rhythmic buildup of low-voltage δ and β range (8–15 Hz) and overlying δ (2–3 Hz) activity is noted in an otherwise normal EEG (arrow). (B) Clear seizure onset is demonstrated with rhythmic δ (2–3 Hz) frequency over the right temporal region with maximum discharge and phase reversal at T6 (arrow). (C, D) Evolution in morphology, increase in frequency, and spread to the left temporal region are seen. Orange bold arrow indicates first signs of bradycardia and slowing to 50 beats per minute (bpm) from baseline 75 to 100 bpm. Red bold arrow subsequently indicates last beat detected and ensuing asystole. (E) High-voltage 1–2 Hz activity is seen diffusely but maximum in the right temporal region, followed by diffuse background attenuation (F). Return of EKG beat is noted by green bold arrow in panel F with return to normal sinus rhythm. Clinical description: (A) Patient is conversing with family. (B, D) She scours the room and continues to appear normal, although formal testing of consciousness was not done. (E) Patient has upward deviation of eyes followed by head drop and loss of tone in the body (black arrow). Patient continues to be unconscious for an additional 30 seconds. She is immediately responsive to questions upon awakening.

(IB and IA are rare occurrences, with IA reportedly occurring in 0.27%–0.4% of monitored epilepsy patients. Seizures in patients with IB and IA have been primarily associated with temporal lobe onset. However, lateralization of such events has not been consistent. It is plausible that seizures involving the temporal lobe result in bradycardia by stimulation of cardiac centers in insula, cingulate cortex, or amygdala. Sudden loss of postural tone usually occurs after at least 8 seconds of IA and manifests as IS. This is often preceded by epileptic auras, automotor or hypermotor activity, or a dyscognitive phase typically seen in frontal or temporal lobe epilepsy. The sequence of events leading to syncope is thought to be seizure activity causing autonomic dysfunction and asystole with resultant generalized cerebral hypoperfusion. Once the seizure ends (whether it is spontaneously or because of the hypoperfusion), normal autonomic function returns and clinical recovery occurs.

Loss of sinus nodal function or sinoatrial block without activation of an underlying escape rhythm is commonly seen in IA. However, progressive atrioventricular block has also been reported. Placement of a cardiac pacemaker is not clearly beneficial, but is common because of the theoretical risk of cardiac arrest, seizure-related falls, and IA being a possible contributory factor to sudden unexplained death in epilepsy.

This case serves as a reminder of the seizure-vs-syncope diagnostic dilemma. It reinforces the idea that IS should be suspected in patients with focal epilepsy presenting with syncopal episodes. Our case was slightly more challenging due to the lack of coexisting seizure-like semiology such as auras and automatisms, and video-EEG was instrumental in making the diagnosis. We used a sequential treatment approach of first optimizing antiepileptic medications in conjunction with cardiac pacing and subsequent surgical resection of the epileptic lesion, and the patient continues to be seizure-free at 18-month follow-up.

**AUTHOR CONTRIBUTIONS**

Dr. Varade: contributed to acquisition of data, analysis and interpretation. Dr. Rajes: contributed to study concept, design, analysis and interpretation. Dr. Bashu: contributed to acquisition of data, analysis and interpretation, revisions and editing, critical review of the manuscript for important intellectual content, study supervision. Dr. Watson: contributed to the critical review of the manuscript for important intellectual content, study supervision.

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**DISCLOSURE**

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

The Resident and 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 and Fellow Section. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
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

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. 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. 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.

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.

Caring for patients with neurologic and neuromuscular 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, meningoencephalitis, 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 Subspecialties), 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. The most recent census of the American Academy of Neurology (AAN) 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%

From the Neurorological Care Unit (J.R.F.D.S., J.A.G.) and Neurocritical Care Fellowship Training Program (J.A.G.), Cerebrovascular Center, Cleveland Clinic Foundation, Cleveland, OH.
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.
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 disease 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 Emergency Neurological 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 neurological 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.

AUTHOR CONTRIBUTIONS
Joa Rocha Ferreira Du Silva, first author, contributed drafting/revising the manuscript for content, including medical writing for content. Juan Antonio Gomes, contributing author, contributed drafting/revising the manuscript for content, including medical writing for content.

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REFERENCES
This R&F Highlights Booklet is also available in PDF format on the iPad® and mobile versions of Neurology!
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.
Reading to children was a source of fulfillment in the life of M.P., a 40-year-old aunt, kindergarten teacher, and reading specialist. Whether in the classroom, the reading room, or the living room, M.P. found joy in the dual role of teacher and storyteller. For her, it was an important means of relating to those under her care. But all of that changed when, on a Thursday morning, M.P. found herself standing at the front of her class and holding in her hands an indecipherable mystery.

It was the attendance sheet. The same sheet she had used for years, and to hear M.P. tell it, it might as well have been covered in hieroglyphs. Moments later, she found that her lesson plans, which she had spent a distinguished career in devising, were equally incomprehensible. By this time, panic had begun to set in, but the watershed moment came as she surveyed the task she had set for herself earlier in the week: Halloween was just around the corner, and she had a classroom to decorate. “I couldn’t figure it out, which is not like me,” she recalls, a sadness creeping into her voice. “How can you not figure out Halloween?”

The school principal was as perplexed as she, and M.P. was promptly discharged from work and into the care of her mother, S.P. Over the next 2 days, new difficulties began to surface. Some were related to her inability to read: for instance, she could no longer tell time. Others manifested themselves in her activities of daily living, as when it took M.P. several hours to pack her travel bag for the move to her mother’s house that Friday.

By Saturday morning, M.P. was having significant problems finding words, and her speech had slowed. When her confusion gave way to anxiety and agitation, S.P. decided that her daughter was going to the emergency room. It was there that, after a fitful day spent in the waiting room, M.P. was first seen by a physician and promptly admitted. Exhausted from her part in the ordeal, S.P. left the hospital and went to sleep.

Not 1 hour went by before her reprieve was interrupted by the phone’s ringing. “I’m screwed!” M.P. exclaimed into the receiver. “It’s a stroke.”

Alexia without agraphia, also commonly referred to as “word blindness,” is a rare neurologic syndrome in which patients lose the ability to read but can still write and comprehend the spoken word. These deficits are also frequently accompanied by a right homonymous hemianopsia, as well as color anomia and various apraxias. It was first described in 1892 by Joseph Jules Déjerine, who hypothesized that this unique pattern of deficits is caused by subcortical lesions that functionally isolate the left angular gyrus, or “language zone,” from the visual cortex. This unique deficit may be brought about by a number of different patterns of lesions, including 1) a single lesion to the splenium of the corpus callosum that stretches posterolaterally so as to interrupt white matter tracts running from the visual cortices of both hemispheres to the left angular gyrus, 2) lesions to both the splenium and the left primary visual cortex, or 3) lesions involving both the splenium and the lateral geniculate nucleus. In each case, the language zone is robbed of its visual inputs but remains intact. Etiologies of these lesions include posterior cerebral artery territory infarct, tumor, or demyelinating disorders such as multiple sclerosis or acute disseminated encephalomyelitis.

M.P.’s alexia without agraphia resulted from biopsy-negative probable primary angiitis of the CNS (figure, A–C). It is noteworthy that these lesions do not interrupt other sensory inputs to the language zone—a fact that M.P. has worked diligently to exploit in the months following her stroke.

Once an avid reader, M.P. was not willing to let her life’s passion go so easily, and she immediately set about teaching herself to read again using all the tools of her profession. One can only imagine her dismay when these efforts met with little success. Recalling her own vexation at her daughter’s situation, S.P. relates, “Ironically, with the knowledge of all these different reading programs—sight words and phonics and all these nuances—it didn’t help her at all with her own disability.” M.P. made use of flash cards with word captions, writing exercises, and a number of other techniques, and while these tools together with occupational therapy aided her in recovering her ability to perform everyday tasks, she was still unable to read.
But where conventional wisdom had failed her, innovation did not, and M.P. soon discovered that her other senses might prove beneficial. Her discovery was this: when shown a word, M.P. could decipher it letter-by-letter with the help of tactile cues such as letter tracing. “She sort of picked up this tactile approach—truthfully—herself,” her mother says with pride. “She’s the one who reinvented the wheel!”

To see this curious adaptation in practice is to witness the very unique and focal nature of her deficit. Given a word, M.P. will direct her attention to the first letter, which she is unable to recognize. She will then place her finger on the letter and begin to trace each letter of the alphabet over it in order until she recognizes that she has traced the letter she is looking at. “That is the letter M,” she declares, after tracing the previous 12 letters of the alphabet with her finger while deciphering a word in front of her. Three letters later, she is able to shorten this exercise with a guess: “This word is ‘mother,’” she announces proudly.

Nor are such intuitions uncommon for M.P. when looking at written words, for although she cannot read a word by sight, it may nevertheless elicit emotions that seem surprisingly appropriate. For instance, when shown the word “dessert” in writing, M.P. exclaimed, “Oooh, I like that!” When shown the word “asparagus”
Resident & Fellow Section: Call for Authors Initiative

Residents and Fellows (R&F) can visit the Call for Authors page and sign up to ‘check out’ a topic: http://neurology.org/site/feature/callfortopic.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 6 weeks of commitment.
Right Brain: How to treat the untreatable

Mr. X came in to the hospital late at night. He initially had left-sided weakness and headache but rapidly progressed to decreased level of consciousness (Glasgow Coma Scale score was 4). From home, I reviewed his head CT, which revealed a large supratentorial bleed that had ruptured into both lateral ventricles, and significant midline shift. Without having seen the patient, I already knew that his prognosis for survival was very low.

I met some of Mr. X’s family in the morning: several of his children were present, though his wife was not. They did not ask many questions, but they understood the severity of the situation. As the family was Hmong, and Mrs. X did not speak any English, the children reported information back to her. I gave them a graphic description of the best-case scenario—that Mr. X would be severely disabled, living in a nursing home, certainly with hemiplegia but likely with speaking difficulty and comprehension problems as well. I also quoted the prognosis from an intracerebral hemorrhage score study and told them that only 3% of patients in his situation survived after 30 days.

The next day I learned that the family’s plan was to consult a shaman. Our team thought that the intention was to perform some sort of farewell ritual for Mr. X prior to withdrawing care for him, similar to other religions performing last rites. However, in my reading, I learned that traditional Hmong spiritual practices have a very different perspective. The shaman’s role was not to say goodbye; rather, the shaman’s role was to heal Mr. X. Traditionally, a Hmong shaman must plead with the spirits of the deceased elders to extend the predetermined lifespan by burning “spirit paper.” When it became clear that this was the family’s intention, we deferred further discussion about goals of care and gave them time to do whatever they felt was needed. We suspected that the shaman would tell them that he would not live, and that the family would soon choose comfort care.

By the end of several days in the intensive care unit, the patient’s neurologic status, which was poor, had stabilized—not worsening, not improving. His other critical care issues were stable, and our team believed that this patient would not likely die from his neurologic insult directly, though the medical issues were still potential threats. Interestingly, the same day, we heard back from the family regarding the shaman’s advice. He had told the family that the previous day would have been an auspicious day to die; however, since Mr. X had had not passed away, he would now be able to survive. Their sources and ours seemed in agreement at that point.

Unfortunately, the shaman’s prediction proved to be premature. In spite of maximal medical therapy, Mr. X’s neurologic status declined. As he approached brain death day by day, I tried to communicate with the family as best as I could. We arranged numerous family meetings and conversations by phone. Despite our coordinated efforts to communicate, the message seemed to be lost in translation. Mrs. X was absolutely certain that her husband was comatose not because of the large bleed in his head, the severe hypertension, or the methamphetamine abuse, but rather, because the spirit of Mr. X’s brother was attacking him for a perceived slight. From her perspective, the doctors, and all their interventions, seemed to be incidental to the primary “treatment”: resolution of the spiritual dispute between Mr. X and his brother. If the dispute were resolved, Mrs. X expected her husband to completely—and immediately—recover.

I was very conflicted while caring for Mr. X. I believed that we were performing painful interventions on him frequently, with no real chance of achieving the goals that the family desired. Even though I explained many times to the family that he would not be able to fully recover, they always deferred to Mrs. X, who in turn took her advice exclusively from the shaman. I asked the family several times to consider comfort care as an alternative method of treating him, because I had lost hope that we were helping him—as did our various attendings and the critical care team helping us. Despite these talks, Mrs. X firmly demanded “everything” be done to keep him alive. She also revealed her greatest fear: if we abandoned him, his spirit would torment her children, much as his brother was tormenting him.

Mr. X continued to decline very slowly but steadily over the next 2 weeks, first showing a “blown” pupil on one side, and later both sides. His neurologic examination started with purposeful movements on his unaffected side, and gradually progressed to bilateral extensor posturing. I knew that there are some patients who do survive Mr. X’s initial presentation; in fact, one of my

From the University of California Davis Medical Center.
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continuity clinic patients was living proof. Nevertheless, it seemed clear to me that at some point, Mr. X lost the chance to be a survivor. Since he could not survive, I wanted to stop hurting him. Although I directly told this to the family, they felt that the facts of the case were outside my understanding altogether, and disregarded my predictions.

The alliance between doctor and patient is typically predicated on the idea that the doctors have special knowledge and skills, and the patient (or representative) trusts the doctor to guide the patient toward health and away from disease. When the patient or family’s belief system is based entirely outside of the structure the physician is working in, what is the role of the physician? Should we have said “Trust us, we know what we are doing”? If so, we would have to claim greater levels of predictive powers than we truly possessed: sometimes the “hopeless” patients do recover, like my clinic patient. Should we have said, “We trust you, tell us what to do”? If so, we would have to claim less knowledge and skill than the amount we are entrusted with to begin with as physicians. In the end, we walked an imaginary middle road where we did what we would do if he were going to survive, and regularly offered comfort care measures as an alternative option. Was that the right approach? It provided the family with some autonomy, and it gave him the best “chance” at surviving that we knew how to give. And yet, it felt somehow wrong, or unfair. If we, the medical team, believed that Mr. X would recover, then we should not have repeatedly offered comfort care measures. On the other hand, if we thought medical treatment was futile, we should not have offered it at all. Because we thought he would die, but were not completely certain of this, we performed this strange procedure of treating him while asking for permission to stop doing so.

In the end, Mr. X did die. His death weights upon me more than others like him. It is hard enough that our job often places us in the impossible position of fighting death itself. For Mr. X, the challenge was amplified because his wife believed that a fully healthy man lay before her, waiting for a family dispute to be resolved. It was my desire to offer him a death free of suffering given that I could not assist in restoring his life. My desire was met with a resistance I had not encountered before, not because the family did not understand, but because the family was not interested in our understanding. At the same time, our role in not “abandoning” him in order to protect his children seemed more important than whatever medical issues we thought we were treating. In effect, our job was to provide spiritual elixir for the children.

There is a degree of cultural sensitivity required of physicians. Sometimes it means that we need to respect a family’s wishes for special death rituals before withdrawing care; other times it means that we need to recognize that withdrawal is not permissible due to religious beliefs. In this case, withdrawal was possible, but only under circumstances governed by a spirit world that we were not privy to.

The small function that a physician can perform while caring for a terminally ill patient is being present and helping the patient and family come to terms with the situation. We were excluded from that entirely, because the family’s belief nullified our role. Did we help him? Did we help the family? Did we perform medically reasonable acts? I still do not know.

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Dr. Goldenholt takes full responsibility for the data, the analyses and interpretation, and the conduct of the research; the author has full access to all of the data; and the author has the right to publish any and all data separate and apart from any sponsor.

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REFERENCES
Teaching NeuroImages & 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: Combined retinal and cerebral hyperperfusion syndrome after carotid thromboendarterectomy

A 62-year-old man presented with mild left hemiparesis, headache, and blurred vision of his right eye. Ten days before, he had undergone thromboendarterectomy because of subtotal stenosis of his right internal carotid artery. MRI revealed confluent white matter edema together with focal hemorrhage consistent with cerebral hyperperfusion syndrome (CHS; figure 1). Likewise, funduscoppy showed small retinal hemorrhages confined to the right eye (figure 2). Under careful blood pressure control, symptoms and brain edema fully resolved within weeks. CHS occurs in around 3% of patients undergoing carotid thromboendarterectomy and can induce severe neurologic deficits. Rarely, hyperperfusion also involves the ipsilateral eye.

AUTHOR CONTRIBUTIONS

From the Departments of Neurology (S.K., M.D., J.B.S., T.H.), Ophthalmology (V.D.-T.), and Neuroradiology (M.W.), University of Aachen, Germany.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
General Submission Instructions

The Resident and 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 and Fellow Section. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
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).

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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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**E-Pearls**

E-Pearls are posted on the AAN and the Neurology R&F website and sent out on a weekly basis to Residents and Fellows via social media. They are composed to be read and absorbed within a few minutes. The editorial team of the Resident & Fellow Section invites E-Pearl submissions. The length should be 85 words or less and include one reference, if applicable. Please submit your E-Pearl to Kathy Pieper at kpieper@neurology.org.

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**MARCH 29, 2013**

**Slow-Flat-Slow**

Paroxysmal loss of consciousness due to syncope is associated with the EEG pattern of ‘slow-flat-slow,’ initially described by Henri Gastaut in 1974. With the onset of cerebral hypoperfusion there is progressive slowing of the background, with disappearance of the alpha rhythm and appearance of theta and delta activity. This slow phase can last for up to 10 seconds and then abruptly disappears, leaving a ‘flat’ EEG. With restoration of cerebral blood flow, the same EEG phenomena occur in reverse order, thereby giving the pattern its name, ‘slow flat slow.’


Submitted by Charles F. Guardia III MD

Disclosures: Dr. Guardia reports no disclosures.

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**AUGUST 5, 2013**

**Ice Cream Headache**

Brain-freeze or cold stimulus headache is an acute, short lasting, frontal non-pulsatile pain that happens in susceptible people upon the passage of a cold stimulus in any form on the palate or the pharynx. Usually it resolves up to five minutes after removing the stimulus. [1] The pathophysiology is not well understood and is thought to be a trigeminal or glossopharyngeal mediated pain. Some studies raised the possibility of a vascular phenomenon that could explain why it is more common in patients with migraine. [2]


Submitted by: Yasir Jassam MD MRCP(UK), PGY2 Neurology, Tufts Medical Center, Boston, Massachusetts.

Disclosure: Dr. Jassam reports no disclosures.

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**SEPTEMBER 11, 2013**

**Quadrantanopia: Parietal vs Occipital**

An inferior quadrantopia can be caused by both a parietal MCA infarct or a PCA infarct affecting the superior bank of the calcarine fissure of the occipital lobe. As most of us know, an occipital lobe infarct largely spares the macula. There are other clues on examination that separate the two etiologies. In parietal visual loss, patients are generally unaware of their deficit and have associated visual neglect. In contrast, patients with PCA infarcts are usually aware of their deficit and do not have visual neglect. Patients with occipital infarcts are able to bisect lines scattered throughout a page and can describe a full picture placed before them, by moving the image to the preserved visual field. These patients also have intact optokinetic nystagmus in contrast to patients with parietal lobe infarcts.


Submitted by Joseph Zachariah, MD, Case Western Reserve, UH Hospitals, Cleveland, OH.

Disclosure: Dr. Zachariah reports no disclosures.

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**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]


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.

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