The second annual Highlights of the Resident and Fellow Section: 2009
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
Monday, April 27, 2009, 5:00-9:00 p.m.
at the Resident & Fellow Career Forum
ANNOUNCEMENT

Neurology® Resident and Fellow Section Writing Award

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 on-line 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 2010 and will be awarded for a paper published in 2009.

No formal application process is required. All manuscripts submitted to the section will be considered. Manuscripts should be submitted on-line at www.neurology.org. Please direct any questions to kpieper@neurology.org.
Welcome Once Again to the Resident and Fellow Section of Neurology!

This second edition of Highlights of the Resident and Fellow Section provides representative examples of some of the finest articles written by neurology trainees during the past year.

The Resident and Fellow Section (RFS) began in January 2004 as an effort both to serve the trainee readership of the journal and to provide an outlet for resident writing. The Section is trainee-run: a team of 12 residents and fellows, each of whom serves for three years, has responsibility for writing, reviewing, editing, and publishing articles of interest to trainees. Photographs and brief biographies of the Resident and Fellow Section Editorial Team follow this introduction.

The Section has several different subsections, as well, which are well-represented by the articles in this booklet. These include Emerging Subspecialties in Neurology, Clinical Reasoning, Right Brain, Child Neurology, Pearls and Oy-sters, International Issues, Education Research and Initiatives, Teaching Neuroimages (including both static images and videos), and Book Reviews. The descriptions of the subsections appear before each sample article.

The group also has responsibility for initiating and developing other unique projects, including podcasts, other electronic communications, a website, and new subsection ideas. Podcasts related to articles published in the RFS began in December 2007, for example, and weekly E-Pearls, or e-mail “pearls,” have been sent to residents nationwide since July 2008. An archive of E-pearls can be found at www.aan.com/go/education/residents/epearl.

The Section is strongly supported by Neurology’s Editor-in-Chief, Dr. John Noseworthy, the Associate Editors, the journal staff, the American Academy of Neurology, and the publishers Lippincott Williams and Wilkins. Neurology recognizes that the future of the journal, and the future of the field of neurology itself, depends on the interest and commitment of its readers and writers. This journal is one of the most important records of our profession, and current trainees are the profession’s most valuable resource.

We anticipate further developments for the RFS in the future, limited only by the imagination of the students, residents, fellows, and others who are interested in neurology education. For example, the first annual RFS Writing Award will be awarded at the time of the 2009 AAN Meeting for the best manuscript published in the Section in 2008. We have also initiated plans to get residents involved in peer review of scientific manuscripts submitted to the journal. Through these efforts, we hope that the Section can play a role in helping trainees to meet requirements for core competencies related to practice-based learning and improvement, communication skills, and professionalism.

We welcome submission of manuscripts for the Resident and Fellow Section, and author instructions can be found at www.neurology.org. Papers submitted for this Section will undergo the same thorough peer review process as all Neurology submissions, and it is anticipated they will reflect the same high level of quality. It is further expected that manuscripts published in the Section will carry the same academic weight, whether on-line or in print, as papers published elsewhere in Neurology. We also continue to welcome input from our readers, including program directors and other educators, on features that will be most valuable. Questions and comments should be addressed to Mitchell Elkind or Kathy Pieper at kpieper@neurology.org.

We hope you enjoy this special second edition of Highlights of the Resident and Fellow Section of Neurology!

Mitchell Elkind, Resident and Fellow Section Editor

Disclosures: Dr. Elkind has no disclosures.
Dr. Elkind graduated from Harvard Medical School in 1992, interned at Brigham and Women’s Hospital, and completed neurology residency at Massachusetts General Hospital. He then obtained a Masters degree in Epidemiology from Columbia University while doing his clinical stroke fellowship. Currently, Dr. Elkind is an Associate Professor of Neurology at Columbia University in the Division of Stroke and the Associate Chairman for Clinical Research and Training. His research is focused on inflammatory and infectious biomarkers in stroke risk prediction, as well as acute stroke therapy. Dr. Elkind is a Principal Investigator of 3 NINDS independent investigator awards. These include NeuSTART (Neuroprotection with Statin Therapy for Acute Recovery Trial), a clinical trial evaluating short-term high-dose statin therapy in acute stroke; Levels of Inflammatory Markers in the Treatment of Stroke (LIMITS), a multi-center blood biomarker study among lacunar stroke patients participating in the SPS3 trial; and the Northern Manhattan Study, a prospective cohort study of stroke risk factors. He is the former Neurology Residency Program Director at Columbia University Medical Center, and is a fellow of the American Academy of Neurology and a member of the American Neurological Association and the Stroke Council of the American Heart Association. He has mentored several residents and fellows in neurology and clinical research.

Megan Alcauskas is the resident editor of Right Brain, the medical humanities segment of the Resident and Fellow Section. Dr. Alcauskas received her BS in Biology from Boston College in 2001 and her MD from Columbia University in 2005. She is currently in her fourth post-graduate year at Mount Sinai Hospital in New York City.

Rajani Ruth Caesar is a PGY 4 and Chief Resident in the Neurology residency program at UTMB Galveston, Texas. She received her medical degree from Erasmus University in Rotterdam, the Netherlands. After two years researching traumatic brain injury at UTSW in Dallas, Texas, Dr. Caesar did an internship in Toledo, Ohio. There she served as Chief Resident in the Transitional Year program. She is the resident Editor for the Book Review Section.

James Berry attended medical school at Northwestern University in Chicago, Illinois, where he earned both a medical doctorate and master’s degree in public health. During medical school he spent one year at UCSF as a Doris Duke Clinical Fellow, designing, conducting, and publishing a study examining the effect of gabapentin on acute herpes zoster pain. Currently, he is a Chief Resident in the Harvard Partners Neurology Residency. He plans to pursue fellowship training in neuromuscular medicine at Harvard Partners starting in June 2009.

Shafali Jeste earned her BA in philosophy from Yale University in 1997, and then her MD from Harvard Medical School in 2002. She completed her child neurology residency at Children’s Hospital, Boston, where she served as the Chief Resident in Neurology in 2006. She has now transitioned from fellowship to attending at Children’s Hospital, Boston, with funding from the Child Neurology Foundation and Autism Speaks. Her clinical and research interests are in autism, with a focus on the creation of neurologically based endophenotypes. She currently is performing a study using ERPs to define neural markers for autism in the Tuberous Sclerosis Complex.

Megan Alcauskas, MD

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Sheng-Han Kuo, MD

Sheng-Han Kuo completed medical school at National Taiwan University in Taipei, Taiwan, and pursued further neurophysiology training at Northwestern University. He currently serves as the chief resident at Baylor College of Medicine. He is interested in translational research in Movement Disorders and will receive further fellowship training at Columbia University in New York City.

John Millichap, MD

John Millichap, MD, is a pediatric neurology fellow at Children’s Memorial Hospital and Northwestern University Medical School. His education includes a bachelor of arts from Northwestern University and a medical doctorate from American University of the Caribbean School of Medicine. His research interests include CNS infections and epilepsy syndromes.

Shanna Patterson, MD

Shanna Patterson is originally from coastal California, where she completed medical school at UCSD. For the last three years she has relished living in New York City and is currently a third year resident in neurology at Columbia University. Recently she has also enjoyed being an active part of the Neurology Resident and Fellow Section’s editorial team, as well as a member of the Podcast Committee. Next year she will be completing a fellowship in Neuromuscular Diseases and EMG at Columbia.

Keith Ridel, MD

Keith Ridel, MD, is a pediatric neurology fellow at Cincinnati Children’s Hospital Medical Center. He completed his undergraduate studies in the classics at the University of Cincinnati and attended the University of Cincinnati College of Medicine. His academic interests include movement disorders and neuroanatomy.

Farrah Mateen, MD

Farrah Mateen is a final year resident in adult neurology at the Mayo Clinic in Rochester, MN. She is originally from Prince Albert, SK, Canada, and completed medical school at the University of Saskatchewan and the Medical Ethics Fellowship at Harvard University. She is especially interested in international issues related to health, neurological disease in underserved populations, and government policies regarding people with chronic illness.

Ryan Overman, MD

Ryan Overman is originally from Anderson, Indiana. He studied chemistry and anthropology at Butler University before attending the Indiana University School of Medicine. There he served his senior year of adult neurology residency as chief resident and graduated in June of 2008. He is now Assistant Professor of Clinical Neurology at the Indiana University School of Medicine. His interests include neurophysiology and localization in neurologic disease.

Sashank Prasad, MD

Sashank Prasad is neuro-ophthalmology fellow at the Hospital of the University of Pennsylvania, where he also completed neurology residency. He attended Yale University, where he majored in English, and the University of Pennsylvania School of Medicine. Next, he will pursue a research fellowship, studying cortical responses to visual loss using functional neuro-imaging.

Sarah Song, MD, MPH

Sarah Song studied English and Women’s Studies at Williams College, and received her MD and MPH from the University of Illinois College of Medicine at Peoria. She is currently a neurology resident at Georgetown University, and will pursue her vascular neurology fellowship at UCLA in 2009. Her academic interests include stroke prevention and stroke epidemiology. She is also a graduate of the 2009 Donald M. Palatucci Advocacy Leadership Forum.
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.
Emerging Subspecialties: Neurorehabilitation
Training neurologists to retrain the brain

WHY NEUROREHABILITATION? If not newly emerging, the subspecialty of neurorehabilitation is definitely burgeoning, and neurology trainees may not be aware of the exciting career opportunities within the field. The contemporary neurology resident is trained in a discipline that has changed dramatically in the last two decades. The modern day neurologist has a slew of treatment options at hand, from t-PA to multiple immunomodulating medications, and practices with this arsenal of treatments from the emergency room to the outpatient clinic. Despite these advances, many patients still leave the hospital or clinic with debilitating cognitive and sensorimotor impairments and ask what we can do to help them walk or use a hand again or regain enough function to return to their ordinary life activities. Some want advice regarding the prevention of further neurologic deterioration.

The discipline of neurorehabilitation is the field concerned with these reminders of past and present neurologic illness and the improvement of neurologic function. Yet it is not uncommon for many neurology residents to get only a glimpse of this discipline, caught perhaps during a short spinal cord or traumatic brain injury rotation. Beyond the first 72 hours of acute stroke care, most residents will have no interaction with patients to help them swallow, walk, reach and grasp, or manage language and hemineglect disorders. For many residents and practicing neurologists, the team-based approach to therapy characteristic of rehabilitation medicine, and the lack of focus on “localize the lesion” discussions, may seem foreign and fail to inspire a vision of their potential role as a neurorehabilitationist.

But it is precisely neurologists’ background knowledge and interests that make them ideal leaders and partners in the neurorehabilitation team. The neurologist’s in-depth understanding of the anatomy, physiology, mechanisms of injury, and plasticity of the nervous system is an essential component both in offering prognostic guidance to patients and families during rehabilitation and in the development of new and more effective techniques to enhance motor control and cognitive skills. The neurologist’s appreciation of how the web of neuromedical complications and symptomatically targeted medications can affect the nervous system is also an important component in managing the course of rehabilitation and helping move the patient and therapy team toward a set of realizable goals.

Beyond this currently available leadership role in neurorehabilitation, the future of the discipline offers young neurologists even more exciting career prospects. From the molecular neurologist to the neurologic ethicist, the “plastic” nervous system is an intriguing target of study. Neurologists with an interest in research are increasingly directing the translation of stem cell neurobiology, fundamental mechanisms of earning, neuropharmacological manipulations, cortical electromagnetic stimulation, robotic therapy, and brain-computer interfaces into ways to improve outcomes. The recent introduction of large scale neuroscientifically based therapeutic clinical trials into the field of rehabilitation is advancing the opportunities for evidence-based patient care. Another aspect of great appeal in neurorehabilitation is that it continues to be grounded within general neurology. The principles of neural repair and plasticity share a basic foundation across and beyond the various pathophysiologic etiologies of the original neural injury, so the neurologist trained in neurorehabilitation may contribute to the care of patients with multiple sclerosis, peripheral neuropathy, traumatic brain injury, stroke, or other diseases. A neurologist who can help them identify spared pathways and enable them to practice a skill will give patients hope and better quality of life. As young soldiers return

From the Human Cortical Physiology Section (M.A.D., L.G.C.), Medical Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, and Brain Research Institute (B.I.D.), Department of Neurology, Geffen School of Medicine, University of California, Los Angeles.

Disclosure: The authors report no conflicts of interest.
from battlefields with the scars of traumatic nervous system injury, or as the aging population suffers cerebrovascular complications in greater numbers, the skills of the neurorehabilitationist will be in even greater demand.

**TRAINING OPPORTUNITIES IN NEUROREHABILITATION** A broad range of training paradigms currently fall under the neurorehabilitation umbrella, from the basic science benchtop laboratory to the outpatient clinic. The American Academy of Neurology (AAN) section on Neural Repair and Rehabilitation has drafted a proposed core curriculum for training [http://www.aan.com/globals/axon/assets/2736.pdf](http://www.aan.com/globals/axon/assets/2736.pdf). Some of the skills that must be learned by the neurorehabilitationist are familiar to neurologists and make them ideal candidates for this role, including understanding the basic science of nervous system plasticity, anticipating the long-term effects of neuromuscular disorders, and managing the medical and social consequences of neurologic injury. However, the neurorehabilitation fellowship is also a chance for the neurologist to learn a new skill set including management of chronic pain, the use of research disability scales, or the completion of formal disability evaluations. Neurorehabilitationists also need to become fluent in the language of occupational, physical, and vocational therapy and to learn how therapists and patients use orthotics or assistive devices, and how these tools fit into the economics of rehabilitation. A set of recommended readings and a certification examination originally established by the American Society of Neurorehabilitation (ASNR) may soon be managed by the United Council for Neurologic Subspecialties. Both the ASNR and the World Federation for Neurorehabilitation sponsor *Neurorehabilitation and Neural Repair*, a bimonthly journal dedicated to the translational clinical sciences of neurorehabilitation. Interested trainees can find listings of current fellowships through the ASNR [http://www.asnr.com/clientuploads/ASNRFellowshipInformationUPDATE.DOC?PHPSESSID=983e2c30d63e57a482c675f427f5390 days](http://www.asnr.com/clientuploads/ASNRFellowshipInformationUPDATE.DOC?PHPSESSID=983e2c30d63e57a482c675f427f5390 days), through the AAN, or through the American Academy of Physical Medicine and Rehabilitation [http://www.aapmr.org/member/felsearch.htm](http://www.aapmr.org/member/felsearch.htm).

As with many smaller subspecialties, residents seeking training in neurorehabilitation need to identify those aspects of training they are most interested in to find a compatible fellowship. While some programs concentrate on the topics covered in the AAN proposed curriculum, preparing a fellow for clinical neurorehabilitation practice in about 1 year, others are aimed more toward academic neurorehabilitation, emphasizing research-based curriculum in areas such as mechanisms of activity-dependent plasticity, functional neuroimaging, transcranial magnetic stimulation, or stem-cell biology, over 2 or more years. Some fellowships may emphasize a disease orientation, such as stroke, brain or spinal cord injury, and multiple sclerosis. Trainees may want to combine general clinical and focused research curricula through one or more fellowships.

**CAREER PROSPECTS IN NEUROREHABILITATION** The career prospects for neurorehabilitationists are as varied as the primary interests that lead them to the field. While general rehabilitation is dominated by physiatrists, neurorehabilitation is really a subspecialty that appeals only to a small subgroup of physiatrists. A brief survey of the nationwide job listing service provided by HealthJobs.com, conducted at the time of this writing, revealed eight positions for neurologists with an interest in rehabilitation and one for physiatrists interested in neurology. Many of these positions are academic, reflecting a trend seen in other parts of the world, where neurologists are ushering in a new era in neurorehabilitation.8

**DISCUSSION** Perhaps we can take inspiration from the neurologist who formally introduced rehabilitation techniques to modern medical practice, Dr. Henrich Sebastian Frenkel. Dr. Frenkel, a Swiss neurologist, astutely observed an improvement in the finger-to-nose examination of one of his patients with tabes dorsalis. Upon further questioning, he learned that the patient, having “failed” the examination in a previous visit, had “practiced” so that he would “pass” at his next appointment.9 Inspired by his patient, Dr. Frenkel began the organization of a field that would lead within a few years to a department of “ré-éducation fonctionnelle” at La Salpêtrière in Paris. The field flourished among neurologists in Europe, and has now led to 20 to 25 academic neurorehabilitation programs in the United States. Now US neurology trainees can increasingly appreciate that a “functional re-education” of our understanding and treatment of the injured nervous system may benefit our patients, our careers, and our profession.

**ACKNOWLEDGMENT**
The authors thank Jane Dimyan-Ehrenfeld for her editing assistance.
REFERENCES

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 2500 words; permission for longer articles will be needed from the editors. The number of references should be ten or less and 1-2 tables or figures can 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 have the same requirements as NeuroImages but are especially valuable to the trainee audience and will be published in the online Resident and Fellow Section. A number of new categories were added in 2007. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
Clinical Reasoning is a new initiative of the Resident and Fellow Section of Neurology. It 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 2-4 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.
Clinical Reasoning:
A 42-year-old man with sequential monocular visual loss

SECTION 1
In April 2005, a 42-year-old African American man developed insidious, painless visual loss in the left eye which quickly progressed over several weeks.

There was no significant medical history. Family history revealed hypertension and diabetes, but no autoimmune disorders, brain tumors, or vision loss. He was a restaurant manager, smoked ½ pack of cigarettes daily, consumed alcohol rarely, and did not use illicit drugs.

He presented to another institution, where he was found to have 20/100 acuity, dyschromatopsia, and a relative afferent pupillary defect in the left eye. The left optic nerve head was mildly swollen, without hemorrhage or exudate.

Humphrey visual fields of the left eye revealed a dense superior altitudinal defect with a less prominent inferior arcuate defect. The right eye field was full.

He was thought to have idiopathic optic neuritis. He was treated briefly with oral corticosteroids, but his vision in the left eye never improved.

Questions for consideration:
1. What are the diagnostic considerations for subacute monocular visual loss in an adult?
2. What diagnostic workup would you perform?
SECTION 2
The differential diagnosis for subacute monocular visual loss is broad. Although idiopathic demyelinating optic neuritis is a common cause, the differential also includes inflammatory and infectious conditions, compression, infiltrative or neoplastic processes, hereditary optic neuropathies, glaucoma, retinal disorders, and ischemic optic neuropathy (table 1).

Optic neuritis. Optic neuritis most often occurs between the ages of 20 to 50 and is three times more frequent in women. Visual loss reaches its nadir within 7 to 10 days and begins to recover within 1 month. Retro-orbital pain, particularly with eye movements, occurs in almost all cases; it may precede the visual loss and typically persists for 1 to 2 weeks.

Characteristic findings on examination support the diagnosis of typical optic neuritis. Visual field defects, such as diffuse field loss or central scotomas, are common. In acute optic neuritis, one-third of patients have mild optic disc swelling; the remainder have retrobulbar inflammation and the optic nerve head will appear normal.

Atypical features should prompt a rigorous search for other causes of monocular visual loss. These “red flags” include an unusual temporal profile (progression beyond 2 weeks, or lack of recovery within 1 month), absence of pain, an unusual scotoma (such as an altitudinal defect), or an atypical funduscopic examination (including a nerve that is markedly swollen or atrophic, or retinal abnormalities such as hemorrhages, inflammation, or exudates).

Other causes of optic neuropathy. Inflammatory conditions are an important cause of subacute optic neuropathy. In sarcoidosis, optic nerve involvement can be accompanied by anterior uveitis or posterior segment vitritis. There is progressive visual loss, which is often steroid-responsive, and significant pain is unusual. Optic neuropathy is also rarely associated with systemic lupus erythematosus and Sjögren disease.

Infectious conditions are another frequent etiology. Neuroretinitis, in which optic neuropathy coexists with peripapillary or macular exudates, may be due to cat scratch disease (Bartonella henselae), syphilis (Treponema pallidum), Lyme disease (Borrelia burgdorferi), or other infectious etiologies. Other infectious causes include HIV and opportunistic infections, including toxoplasmosis, cytomegalovirus, and cryptococcus. Paranasal sinusitis or mucocele can lead to compressive or inflammatory optic neuropathy.

A variety of compressive mass lesions can cause a progressive optic neuropathy. Important causes include neoplasm (including optic nerve sheath or skull base meningioma, pituitary adenoma, and cranio-phyngioma), sinus lesions, bony processes (fibrous

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<th>Table 1</th>
<th>Differential diagnosis for subacute monocular visual loss</th>
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<td><strong>Condition</strong></td>
<td><strong>Types</strong></td>
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<tr>
<td>Optic neuritis</td>
<td>Idiopathic optic neuritis, multiple sclerosis</td>
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<tr>
<td>Ischemic optic neuropathy</td>
<td>Arteritis, nonarteritic ischemic optic neuropathy</td>
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<tr>
<td>Inflammatory optic neuropathy</td>
<td>Sarcoidosis, systemic lupus erythematosus, Sjögren syndrome</td>
</tr>
<tr>
<td>Infectious optic neuropathy</td>
<td>Paranasal sinusitis, cat scratch disease (Bartonella henselae), syphilis (Treponema pallidum), Lyme disease (Borrelia burgdorferi), toxoplasmosis, cytomegalovirus, cryptococcus</td>
</tr>
<tr>
<td>Compression</td>
<td>Paranasal mucocele, meningioma (optic nerve sheath or skull base), bony compression (fibrous dysplasia), enlarged extracocular muscles, aneurysms</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>Optic nerve glioma, optic nerve glioblastoma multiforme, lymphoma, leukemia, carcinomatous meningitis, metastasis</td>
</tr>
<tr>
<td>Hereditary</td>
<td>Leber hereditary optic neuropathy</td>
</tr>
<tr>
<td>Glaucomatous</td>
<td>Chronic glaucoma, acute angle closure glaucoma</td>
</tr>
<tr>
<td>Retinal</td>
<td>Chronic serous choriorretinopathy (CSR), retinal artery occlusion (RAO), retinal vein occlusion (RVO), acute idiopathic blind spot enlargement syndrome (ABSE)</td>
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Table 2  Diagnostic testing considerations

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<th>Imaging</th>
<th>MRI brain and orbits, optical coherence tomography, fluorescein angiography</th>
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<td>NMO-IgG, RPR, titers for Lyme, toxoplasmosis, Bartonella henselae, West Nile virus (WNV), HIV, herpes simplex virus (HSV), angiotensin converting enzyme, antinuclear antibodies, SS-a, SS-b; lumbar puncture for cell counts, protein, glucose, oligoclonal bands, and PCR for Lyme, HSV, WNV</td>
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<tr>
<td>Genetic testing</td>
<td>Leber hereditary optic neuropathy mitochondrial DNA testing</td>
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<td>Electrophysiology</td>
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dysplasia), enlarged extraocular muscles, or aneurysms. Primary neoplasms include benign optic nerve glioma in children, and rarely malignant glioblastoma in adults. Other neoplastic conditions include lymphoma, leukemia, carcinomatous meningitis, and optic nerve metastasis.

Among the hereditary causes, Leber hereditary optic neuropathy is most common. It often becomes bilateral and the visual impairment is usually severe. There is maternal inheritance, with variable penetrance within families. The condition arises from mitochondrial DNA mutations that impair cellular energy stores. Most cases affect men, but the reasons for this gender asymmetry are unclear. The absence of pain in Leber hereditary optic neuropathy can serve as an important distinguishing feature. Findings on examination may include circumpalpebral telangiectatic microangiopathy and pseudoedema of the nerve fiber layer.

Glaucomatous optic neuropathy is typically easily distinguished from optic neuritis, since it occurs in the setting of elevated intraocular pressure and optic disc cupping. However, angle closure glaucoma may present with painful acute visual loss, resembling the features of optic neuritis. Distinguishing characteristics include the severity of pain (which can be excruciating) and a red eye with an enlarged, nonreactive pupil.

A number of retinal conditions may present with symptoms similar to optic neuritis. These patients will often describe metamorphopsia (distorted or bent images) or photopsia (sparkles of light). Furthermore, there are often distinctive retinal findings. In acute idiopathic blind spot enlargement syndrome, examination reveals peripapillary pigmentary changes without disc swelling. Central serous choroidopathy, which predominantly affects young men with a type A personality, presents with acute, painless visual loss due to macular retinal detachment. The hallmark of retinal artery occlusion is retinal whitening, and that of retinal vein occlusion is retinal hemorrhage and engorgement of retinal veins.

The clinical profile of nonarteritic ischemic optic neuropathy may occasionally overlap the findings of optic neuritis. Features that favor ischemic optic neuropathy in the appropriate clinical setting include nerve fiber hemorrhages, altitudinal visual field loss, moderate to severe disc edema, and the absence of pain. Vascular risk factors such as age, hypertension, diabetes, or hyperlipidemia are often present. Moreover, most patients with nonarteritic ischemic optic neuropathy have the anatomic predisposition of a small cup to disc ratio.

Diagnostic workup. Once the differential diagnosis has been narrowed on the basis of the clinical history and physical examination, an appropriate diagnostic workup is imperative to confirming the correct diagnosis (table 2).

All patients with typical optic neuritis should undergo brain MRI to assess the risk of multiple sclerosis. MRI of the orbits may confirm optic nerve enhancement in the majority of patients with optic neuritis and may be helpful to exclude alternative causes of optic neuropathy. Testing for NMO-IgG (neuromyelitis optica anti-aquaporin-4 antibody) is useful in patients with recurrent, bilateral, or severe optic neuritis, especially in patients with longitudinally extensive transverse myelitis.

In the routine case of optic neuritis, serologic tests are of limited diagnostic value. However, in patients with atypical or systemic features, serum testing may be considered for syphilis, Lyme disease, toxoplasmosis, cat scratch fever, West Nile virus, HIV infection, and herpesvirus infection, as well as serum angiotensin converting enzyme level, antinuclear antibodies, and Sjögren antibodies. In cases of suspected inflammatory or infectious optic neuropathy, lumbar puncture is necessary.

Genetic testing for Leber optic neuropathy is useful in patients with painless visual loss that is severe or bilateral, particularly if they are young men.

Visual evoked potentials are not routinely used in the diagnosis of demyelinating optic neuritis, although the finding of a P100 response with prolonged latency provides evidence for optic nerve demyelination. Testing may be helpful when there is a question of retinal disease vs optic neuritis or when subclinical optic neuritis is suspected.
An electroretinogram may be helpful in patients with suspected retinal dystrophy, paraneoplastic retinopathy, retinal artery occlusion, or a retinal inflammatory process. Likewise, fluorescein angiography may also confirm retinal inflammatory or ischemic processes. Optical coherence tomography (OCT) is usually normal in acute optic neuritis, but may be helpful in distinguishing some retinal conditions.

Clinical course. An MRI of the brain was obtained at the initial presentation. It revealed an enlarged and enhancing left optic nerve, and was thought to be consistent with the presumed diagnosis of optic neuritis (figure 1).

In September 2005 (6 months after the initial presentation), the vision in the left eye had progressed to no light perception. A follow-up MRI revealed increased left optic nerve enlargement, with extension into the chiasm and pathologic enhancement. At another institution, a presumptive diagnosis of a left optic nerve glioma was made on the basis of clinical and radiographic progression. Neither biopsy nor resection was considered feasible due to chiasmal involvement, and he was treated empirically with proton beam therapy (50 Gy equivalent, January 2006–March 2006) and temozolomide (March 2006–May 2007). He tolerated the therapy well, but there was no clinical improvement. Serial MRIs demonstrated stability of the left optic nerve lesion, with resolution of enhancement.

In May 2007 (25 months after the initial symptoms), he presented to our institution and reported 2 weeks of painless vision loss in the previously unaffected right eye. He perceived cloudiness over the entire visual field. The left eye remained no light perception. Associated symptoms included mild headache, fatigue, decreased appetite, mildly impaired concentration, and frequent epistaxis. He denied weakness, numbness, dysarthria, fevers, rash, arthralgia, or cough.

Medical examination, including detailed skin examination, was normal. Mental status was normal. He had no light perception in the left eye and 20/30 acuity in the right eye which did not improve with pinhole. He saw 10/10 color plates with the right eye. There was a large left relative afferent pupillary defect. He had small arcuate field defects in the right eye visual field. There was optic nerve pallor bilaterally (left greater than right). There was no uveitis. There was a mild comitant exotropia, with full ocular ductions, and normal saccades and pursuit. There was no ptosis or nystagmus. The remainder of the neurologic examination was normal.

Questions for consideration:
1. What are the diagnostic considerations for bilateral sequential monocular visual loss?
2. What diagnostic workup would you pursue?
SECTION 3

The differential diagnosis for bilateral sequential monocular visual loss includes many of the causes described above, including inflammatory, neoplastic, and infectious etiologies. Sarcoïdosis, for example, may affect additional sites in the nervous system, including the contralateral optic nerve. In cases of treated neoplastic optic neuropathy, the distinction between radiation optic neuropathy and tumor recurrence can sometimes be challenging. Radiation optic neuropathy is suggested by exposure (to 50 Gy), characteristic 18 to 36 month lag time to symptoms, and radiation changes in proximal tissues. Bilateral visual loss in a patient with known or suspected cancer raises the possibility of a paraneoplastic retinopathy or, less commonly, optic neuropathy. In paraneoplastic optic neuropathy, there is often evidence of other neurologic dysfunction, and the antibody most commonly identified is directed toward collapsing response mediated protein (CRMP 5). The asymmetric and sequential visual loss of our patient coupled with the enlarged, enhancing optic nerves make other conditions such as toxic/nutritional optic neuropathy or hereditary optic neuropathy unlikely.

Clinical course. The patient was admitted for evaluation and treatment of right eye visual loss. Laboratory evaluation revealed a negative or normal metabolic profile, cell counts, erythrocyte sedimentation rate (2 mm/hour), c-reactive protein, angiotensin converting enzyme level (34 units/L), antinuclear antibodies, ANCA, SSA/B, serum protein electrophoresis, thyroid stimulating hormone, and B12 level. The spinal fluid showed 1 wbc/mm³, 0 rbc/mm³, 42 mg/dL protein, 60 mg/dL glucose, no oligoclonal bands, and negative cytology.

MRI of the brain and orbits revealed enlargement and enhancement of the right optic nerve (figure 2). No additional lesions were identified in the brain.

CT scan of the chest and abdomen were essentially normal, without evidence of malignancy or hilar adenopathy (figure 3). PET scan revealed mildly hypermetabolic lymph nodes in the bilateral hila (maximum SUV 3.4–4.2) and mediastinum (maximum SUV 1.5–3.5), inguinal lymph nodes (maximum SUV 1.6–1.7), and prostate (figure 3). There were no hypermetabolic regions in the head or neck, including the optic nerve.

Questions for consideration:

1. On the basis of these results, what additional tests will likely yield the diagnosis?
2. What is the prognosis and optimal treatment of this condition?
Figure 3  Normal CT scan of the chest, axial slice (top), and increased hilar uptake on PET indicating increased metabolism (arrows)

CT

FDG-PET

SECTION 4

Tissue diagnosis was sought to confirm the etiology of the patient’s vision loss because serology, CSF analysis, and imaging studies were largely unrevealing. The left optic nerve was selected because of the longstanding no light perception vision and the high signal abnormality on MRI.

Optic nerve sections showed severe atrophy and gliosis with virtually no axonal elements (Figure 4, top left and top middle panels). There were very few inflammatory cells and no granulomas. Gil Al fibrillary acid protein immunohistochemical stains were diffusely positive, without demonstration of piloid morphology characteristic of glioma (top right panel). Ki67 stain did not show increased proliferation. Hemosiderin deposition was present, likely secondary to radiation and chemotherapy exposure. The previous diagnosis of an optic nerve glioma could not be confirmed.

Findings at PET scanning, including hypermetabolic mediastinal lymph nodes, presented a second-ary site amenable to tissue sampling. Transbronchial biopsy was performed and showed several well-formed, noncaseating granulomas comprised of clusters of epithelioid macrophages and multinucleated giant cells (Figure 4, bottom panels). Grocott and acid fast stains were negative for fungal and acid fast organisms. Noncaseating granulomas, in the absence of an infectious etiology, support the diagnosis of sarcoidosis.

DISCUSSION Sarcoidosis is an uncommon disease characterized by granulomatous inflammation, likely caused by both genetic and environmental factors.

While the lung and skin are most commonly affected, approximately 5% of patients will have neurologic involvement. Neurosarcoidosis has tremendous clinical heterogeneity, which poses diagnostic and therapeutic challenges. The most commonly affected sites are the leptomeninges and cranial nerves, with a predilection for the facial and optic nerves. Involvement of brain and spinal cord parenchyma, pituitary gland, peripheral nerves, and muscle also occurs.

Definitive diagnosis of neurosarcoidosis requires pathologic demonstration of noncaseating epithelioid cell granulomas, an inflammatory neurologic lesion on imaging or CSF analysis, and exclusion of other etiologies. Because there is frequently no neurologic lesion amenable to biopsy, a common alternative strategy is to demonstrate systemic sarcoidosis by biopsy of another organ and to imply the diagnosis of neurosarcoidosis. Potential biopsy sites can be identified by clinical examination or PET, gallium, or MRI scans that screen for clinical or subclinical inflammation. If positive tissue pathology is not available, diagnostic support can be provided by typical systemic symptoms, typical pulmonary radiographic findings and lymphocyte subpopulation ratios in bronchoalveolar lavage fluid. Unfortunately many of these tests are characterized by poor sensitivity and specificity. A variety of diagnostic algorithms using this ancillary data have been proposed, but none have come into widespread use. Therefore, when there is high clinical suspicion, unrevealing studies should not dissuade the practitioner from the diagnosis.

Once a diagnosis of neurosarcoidosis has been made consideration should be given to screening for subclinical involvement of other organs. An initial screening workup should include chest x-ray, pulmonary function tests, complete blood count, creatinine, BUN, calcium, liver enzymes, urinalysis, EEG, ophthalmologic examination, tuberculin skin test, and additional testing guided by abnormalities detected on history and physical examination.

Neurosarcoidosis often requires aggressive treatment focused on controlling symptoms and reducing inflammation. Symptomatic therapy in neurosarcoidosis may...
include antiepileptic agents, pain medication, hormonal replacement therapy, and surgical treatment of hydrocephalus. Disease-controlling therapies aim to blunt the autoimmune response and decrease pathologic inflammation. The mainstay of therapy is high-dose oral corticosteroids for 6–8 weeks, with a preceding pulse of IV corticosteroids if needed. The clinical response should guide a reduction or escalation of therapy. Escalating therapeutic options include steroid-sparing cytotoxic agents, such as methotrexate, azathioprine, cyclophosphamide, and mycophenolate. Other therapies that may have a role include cytokine modulators such as infliximab or thalidomide and antimicrobial agents such as chloroquine or minocycline. Radiotherapy is reserved as a third line therapeutic option. Unfortunately there are no prospective trials to guide the optimal treatment regimen for neurosarcoidosis. Therapy selection is based on comorbidities, expected toxicities, and physician experience. Chronic management should focus on continued escalation or reduction in therapy as guided by progression or remission of symptoms, imaging, and laboratory data. Therefore frequent surveillance is imperative. This should be coupled with appropriate monitoring for therapeutic toxicity.

Clinical course. The patient was treated with high-dose IV methylprednisolone for 5 days, followed by a prolonged taper of oral prednisone. Visual acuity in his right eye normalized. Four months later, while on a tapering dose of prednisone, the patient experienced recurrent right eye visual loss. This prompted the addition of mycophenolate mofetil to the treatment regimen. On combination therapy, the patient’s vision stabilized, allowing further tapering of the oral prednisone.

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

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She was sobbing. Her husband, eyes lowered, turned his head slowly in disapproving judgment. With his tan-colored hat affixed tightly to his tan-colored head, he slouched further in his seat. David, also slouched on the patient table, seemed completely uninterested in the parental affair. He had his own tension. Head bowed, he desperately clutched his flexed right hand with his left. This was my first visit. These were the Almady.

“How are you feeling?” I asked, hoping to break the tension. David only shrugged his shoulders. “All right, I guess,” he replied, his impossibly oversized t-shirt draped over his bony, 14-year-old shoulders. Six months ago, David had suffered a left basal ganglia stroke related to an internal carotid artery dissection. Three months later he arrived at the emergency department complaining of severe arm pain. Imaging suggested a possible second stroke. One month ago he developed a significant dystonia in his right arm. And on the day of the sobbing, I began a longitudinal program at my medical school which paired medical students with physician mentors and their patients.

David’s examination was revealing. As he walked down the hallway his right arm twisted behind him. His left hand, a compassionate figure, reached out to grab his right wrist. “David, put your left hand by your side,” the physician said gently. With that instruction, we watched as his right hand lifted away from his body, now freely subject to the whims of his dysfunctional left basal nuclei. For David, it was not a pleasant liberation. With his left arm hanging loosely by his side, the contralateral nature of the brain had never been so apparent.

The medications were clearly not working. David had lost 30 pounds since the stroke, Mom was emotionally unstable, and Dad was not engaged. The previous week, the family had seen a psychiatrist—someone on the father’s health plan—who discontinued the Klonopin without consulting any of David’s physicians. “Oh, and we can’t really do physical therapy because his father’s insurance doesn’t cover that.” Never had the complexity of illness been so apparent.

Before David’s stroke, he and his father were, as his mother once said, “almost like the same person. You couldn’t separate them.” In particular, Mr. Almady’s memory of his son before the stroke was inextricably bound up with athletics. “He was an athlete. Basketball, football, whatever,” he would tell me at one of David’s visits, the glimmer in his eyes betraying the joy that must have been. For him, David’s dystonia and subsequent movement limitations represented a uniquely existential challenge—an event which demanded a fundamental reconceptualization of who David was.

Illness has a peculiar way of pressing—sometimes gently and oftentimes forcefully—on the fibrous fabric of our lives. And with time, the illness—or rather the meaning that the illness comes to represent—becomes deeply enmeshed into the fabric itself. During that process there are often tears in the fibers that were, perhaps, already frayed.

There were signs. At first, they failed to return my phone calls—six of them. Then, their home phone number changed. I would later learn that Mr. Almady was having an extramarital affair. His female companion was calling the home in what, according to Mrs. Almady, “was nothing but disrespectful to me. And then David found out about it.” Since the affair, I have watched David’s relationship with his father progressively deteriorate. And as the dystonia worsens, it is almost as if David is carrying the mounting tension of his life in his painfully clenched right hand.

For David, the fabric of his life remains largely unknown. Often unable to inspire clarity or reflection from David, I often find myself discussing...
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 2500 words; permission for longer articles will be needed from the editors. The number of references should be ten or less and 1-2 tables or figures can 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 have the same requirements as NeuroImages but are especially valuable to the trainee audience and will be published in the online Resident and Fellow Section. A number of new categories were added in 2007. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.

REFERENCE
A new child neurology section in the Resident and Fellow Section of Neurology will focus 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.
Emerging Subspecialties in Neurology: Building a career and a field
Pediatric neurocritical care

Kerri L. LaRovere, MD
James J. Riviello, Jr., MD

The specialty of neurocritical care (NCC) has evolved rapidly and has an exciting future. The current neurologic intensive care units (NICUs) were born in the 1960s as a collaborative effort among the various subspecialists caring for patients with neurologic illnesses in multidisciplinary intensive care units (ICUs). The first dedicated NICUs appeared in the mid-1970s, and training programs soon followed. There are now 50 dedicated NICUs run by fellowship-trained neurointensivists in 29 states, and 15 hospitals in which neurointensivists provide consultant services. Dedicated NICUs have permitted many advances in basic science, diagnostic, monitoring, and therapeutic techniques in NCC.

Neurointensivists apply the basic principles of neuroresuscitation, the ABCs (airway, breathing, and circulation/cerebral blood flow), to the management of acute, life-threatening brain and spinal cord insults or “failure.” Common diagnoses in the adult NICU include postoperative tumor, stroke, subarachnoid hemorrhage, traumatic brain injury, and intracerebral hemorrhage. Successful management depends upon properly diagnosing, monitoring, and treating these conditions, as well as upon preventing and treating any secondary complications, namely disturbances of cerebral perfusion and intracranial pressure. The clinical and scientific progress in this new specialty has spawned the international Neurocritical Care Society; a peer-reviewed scientific journal, Neurocritical Care; and the approval of NCC for subspecialty certification by an independent, nonprofit professional medical organization, the United Council for Neurologic Subspecialties (UCNS). The next step is certification by the Accreditation Council for Graduate Medical Education, which will signify general acceptance of NCC.

We were drawn to pediatric NCC during our pediatric neurology training because of an interest in managing acute neurologic insults. Moreover, NCC is a new frontier in clinical child neurology with unlimited opportunities for research. Recent collaborative efforts have produced several evidence-based guidelines for the field. In 2000, a working group assembled by the International Brain Injury Association created guidelines for severe pediatric head trauma, with the hope that standardized management of pediatric traumatic brain injury will allow outcome analyses intended to improve current therapies. Guidelines from the United States and United Kingdom have been developed for arterial ischemic stroke and cerebral sinovenous thrombosis in children, and the International Pediatric Stroke Study has created an international stroke registry in an effort to develop true evidence-based practice standards and perform future clinical trials. In addition, the American Academy of Neurology and Child Neurology Society developed a practice parameter for the Diagnostic Assessment of the Child with Status Epilepticus.

As in adult NCC, additional pediatric research topics include age-specific and disease-specific studies related to measurements of cerebral blood flow and intracranial pressure; determinations of clinical, biologic, neurophysiologic, radiologic, and pathologic markers of CNS injury; therapeutic effects on outcome; and factors important in recovery of function. Unlike that of adult NCC, the research agenda in children has a critical additional layer: understanding the response of the developing brain to acute and severe CNS injury. However, pediatric NCC lags behind adult NCC. The field of pediatric neurology does not yet have dedicated pediatric NICUs or training programs, and to date, pediatric NCC has been driven forward by work that has “trickled down” from adult NICUs or from neonatal neurology.

In the current practice of pediatric NCC, the pediatric neurologist functions as a consultant to the pediatric ICU (PICU) team in the evaluation and treatment of acute ischemic stroke, intracere-
bral hemorrhage, traumatic brain injury, anoxic brain injury, status epilepticus, CNS infections, autoimmune and postinfectious disorders, neuromuscular emergencies, neurometabolic crises, postoperative CNS tumors and epilepsy surgery, neurologic complications of general medical and surgical illnesses, and brain death. A multidisciplinary approach is needed to best care for these children. The pediatric neurologist is needed in the PICU as an expert in the neurologic history and examination of a child, an invaluable skill necessary for decision-making and determining prognostic variables. Furthermore, PICUs need the pediatric neurologist because many of the neurologic disorders of these children are chronic, unlike those of their adult counterparts. A pediatric neurologist on the PICU team will provide the best neurologic care for these children.

To establish this frontier, the Department of Neurology at Children's Hospital Boston, under Dr. Joseph Volfpe, created a dedicated critical care neurology service in 1996. All neurology consultations in the medical/surgical PICU, the cardiac intensive care unit, and three neonatal intensive care units are performed by a dedicated critical care neurology team distinct from the inpatient neurology consult team. This service was created because it became difficult to obtain a general neurology consult service to incorporate the many advances in neonatal neurology and NCC into clinical practice. In 2006, this service provided 557 new consults and 3,339 follow-up consultations. Our group includes pediatric neurologists specializing in epilepsy and in neurovascular, neuromuscular, behavioral, and neonatal neurology, but only one had an anesthesiology background. We believe that in order to move our field forward in a manner similar to that of our adult counterparts, we now need to train dedicated pediatric NCC specialists. Presently, the Neurocritical Care Society is planning a workforce evaluation for pediatric NCC, which will be important for developing the field and for identifying funding strategies for training programs.

Several models of pediatric NCC delivery are possible. The most common model is an inpatient neurology consult service providing neurologic consultations to all inpatients. An alternative is the current Boston model, where a dedicated group of neurologists work as consultants to the PICU team. This requires a large neurology department or division. The ultimate model is the creation of a dedicated pediatric NICU staffed with NCC-trained pediatric neurologists, similar to the adult situation. However, the staff at our institution currently does not have the training, experience, or support personnel needed to function as primary attending physicians in a pediatric NICU. Given the current practice of pediatric critical care medicine, where the PICUs in major children's hospitals are closed units staffed by pediatric critical care medicine specialists, pediatric neurologists will most likely remain as consultants to this group. We believe that the best care ultimately will be delivered in a dedicated pediatric NICU staffed by a team consisting of pediatric intensivists and pediatric neurointensivists. In any model, evidence-based treatment guidelines are needed to standardize care and evaluate outcomes.

We believe it is time to move away from recruiting child neurology subspecialists who have a critical care interest to the NCC team, and instead to develop properly trained pediatric NCC subspecialists. The dedicated pediatric neurointensivist would be a member of the PICU team and help perform research on neurologic disorders in the PICU. This model should lead to increased educational efforts in neurointensive and non-neurointensive care, effective collaboration with other caregivers in the ICU, and more efficient care for children with critical neurologic illnesses. Collaboration with other neurologic subspecialists on the NCC team would continue, since epilepsy, neurovascular, and neuromuscular disorders are frequently seen in the ICU.

The pediatric neurointensivist should have training and knowledge beyond pediatric neurology residency. In accordance with the UCNS guidelines for fellowship program requirements (http://www.ucns.org/accreditation), fellows must complete 12 months of on-service critical care training involving the direct diagnosis and management of critically ill neurologic patients, and 12 months of various non-critical care clinical rotations. For pediatric NCC, membership on a team in a medical/surgical PICU, pediatric cardiac intensive care unit, postanesthesia care unit, and adult NICU may count toward the 12-month on-service critical care requirement. Possible non-critical care electives include pediatric neurovascular or stroke service, epilepsy, neurosurgery, emergency department, interventional/diagnostic neuroradiology, Doppler lab, clinical neurophysiology, and research. In particular, training in applications and interpretation of pediatric EEG, continuous EEG, and neuroimaging and neuro-monitoring devices including transcranial Doppler would be useful.

Foundations for a good pediatric NCC program include emphasis on general and neurologic
intensive care through exposure to adult and pediatric general and neurologic ICUs in institutions with interested colleagues and opportunities for clinical and laboratory research. A committee of clinical and research mentors from pediatric neurology, as well as from all parent specialties in critical care medicine, anesthesiology, adult NCC, and neurosurgery, are paramount to future success. Institutions with well-developed ICUs and robust neurology services should consider devising a program. Post-residency (pediatric neurology or anesthesiology) training programs could consider fellowship training integrated with general and neurologic PICU and adult NICU/vascular neurology. Another possibility may be cross training of pediatric NICU specialists during residency with an effort to follow fellowship or practice track pathways (http://www.ucns.org/certification/requirements/neuroint) so that eligibility for the NCC certifying examination is possible.

The Department of Neurology at Children’s Hospital Boston, under Dr. Scott Pomeroy, has established a pediatric NCC fellowship training program in conjunction with the adult vascular and NCC program at Massachusetts General Hospital/Brigham and Women’s Hospital and the anesthesiology/pediatric critical care program at Children’s Hospital Boston. To our knowledge, this is the first and only such program in existence. The first year is a mixture of electives and service time in adult NCC with overnight adult NCC and stroke call. The second year consists of service time in pediatric critical care with rotations in anesthesia, cardiac intensive care, and PICU, and various pediatric non-critical care electives. These 2 years are structured according to the practice track pathway put forth by the UCNS. This program is funded by the Neurology Department in recognition of the need to provide this service to the many children we care for with acute and severe neurologic conditions, as well as the need to train future pediatric neurointensivists. Perhaps other major children’s hospitals will recognize these needs as well, and create similar training programs.

Fellowship directories in NCC can be found on the UCNS Web site at http://www.ucns.org as well as through the American Academy of Neurology at http://www.aan.com/education/fellowships. A list of pediatric critical care medicine fellowships is available on the pediatric critical care Web site at http://pedscm.org. Fellowship funding may be difficult to find. Funds or grants to consider include those available from the government (http://www.grants.gov), such as the National Institute of Neurological Disorders and Stroke (http://www.ninds.nih.gov) and the National Institute of Child Health and Human development (http://www.nichd.nih.gov). Other funding sources may come from major professional organizations such as the Child Neurology Foundation (http://www.childneurologyfoundation.org), American Neurological Association (http://www.aneroa.org), Association of University Professors of Neurology (http://www.aupn.org), Pediatric Critical Care Medicine, and the American Academy of Pediatrics (http://www.aap.org).

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REFERENCES
Teaching NeuroImage: Hemiconvulsion-hemiplegia-epilepsy syndrome
Sequential MRI follow-up

A 42-month-old boy presented with frequent left partial motor seizures of 3 months duration. The symptoms began after an acute episode of fever, encephalopathy, vomiting, and left partial seizures lasting 1 week. CSF was unremarkable and negative for HSV PCR. Evaluation for procoagulant states was negative. He recovered with left hemiparesis. MRI during the acute illness (Figure 1) and at 3 months (Figure 2) suggested a diagnosis of hemiconvulsion-hemiplegia-epilepsy (HHE) syndrome.

HHE syndrome is characterized by prolonged unilateral convulsions with fever in children under 4 years of age, who subsequently develop hemiplegia, partial epilepsy, and extensive atrophy of the involved hemisphere. The pathogenesis is believed to be an interplay among genetic predisposition; viral infection (e.g., influenza, HHV 6) or toxin (theophylline) exposure; excitotoxicity due to prolonged ictal activity; and contributory systemic factors such as cytokine excess, hypoxia, ischemia, and fever.

REFERENCES

Figure 1  T1 axial (A), T2 axial (B), and coronal (C) (FLAIR) sections of brain show thickening of cortical gray matter with increased signal intensity on T2W and FLAIR images with effacement of sulcal spaces and midline shift suggestive of unilateral encephalitis.

Figure 2  T1 axial (A), T2 axial (B), and coronal (C) (T2) sections of brain showing right hemispherical atrophy with gliotic changes and ventricular dilation, as well as right subdural hematoma.

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PEARLS AND OY-STERS

“Pearls and Oy-sters” is a new feature of the Resident and Fellow Section of Neurology that will focus on fundamental clinical neurology. Each article should address 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. The article should 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:
The medial longitudinal fasciculus in ocular motor physiology

ABSTRACT

Objective: To review the role played by the medial longitudinal fasciculus (MLF) in ocular motor physiology and to characterize a number of syndromes that result from lesions in this eloquent brainstem tract system.

Background: The MLF is responsible for transmitting information that is crucial for the coordination and synchronization of all major classes of eye movements. A number of disease processes can produce lesions within this small yet highly strategic white matter pathway resulting in a myriad of neuro-ophthalmologic signs and symptoms.

Methods: We carefully reviewed both the literature and our collective experiences to systematically consider the neuroanatomy and physiology of the MLF and the pathophyslogic mechanisms that underlie syndromes deriving from lesions in this pathway.

Results: The MLF is an important structure and is composed of numerous projection systems involved in the regulation of eye movements. Pathology at this location can produce a constellation of abnormalities, many of which can be identified upon careful bedside neurologic examination.

Conclusion: This review of the medial longitudinal fasciculus and its constituent pathways is germane to understanding a number of important principles in neuro-ophthalmology. *Neurology* 2008;70:e57–e67

GLOSSARY

FEF = frontal eye field; FPA = first-pass amplitude; INC = interstitial nucleus of Cajal; INO = internuclear ophthalmoplegia; MLF = medial longitudinal fasciculus; MS = multiple sclerosis; NPH = nucleus preopticus hypoglossi; NRTP = nucleus reticularis tegmenti pontis; OD = right eye; OS = left eye; OTR = oculo-tilt reaction; PPFR = paramedian pontine reticular formation; PSP = progressive supranuclear palsy; r-VOR = rotational vestibular ocular reflex; rMLF = rostral interstitial nucleus of the MLF; SC = superior colliculus; SVN = superior vestibular nucleus; VDI = versional disconjugacy index; VLVN = ventral lateral vestibular nucleus.

The medial longitudinal fasciculus (MLF) is organized as a pair of white matter fiber tracts that extend through the brainstem and lie near the midline just ventral to the fourth ventricle (in the medulla and pons) and cerebral aqueduct (in the midbrain). The MLF contains fibers that ascend and some that descend through the brainstem tegmentum and interact with ocular motor control circuitries involved in the coordination of horizontal, vertical, and torsional eye movements.1,2

The MLF is a central conduit for many brainstem pathways and is the final common pathway for all classes of conjugate eye movements including saccades (rapid reflexions), smooth pursuit, and vestibuloocular reflexes, including semicircular and otothyl mediated ocular motor reflexes. The six ocu-
lar motor nuclei (pairs of cranial nerve III, IV, VI) are interconnected via the MLF, which transmits vital information for the purpose of coordinated and synchronized movements of the eyes to a visual target. Within this system are both excitatory as well as reciprocal inhibitory projections that serve to precisely regulate the interplay between agonist and antagonist muscles of the eyes.

In this review, we characterize the physiology of the component tract systems contained within this central ocular motor circuitry, and provide a detailed discussion of the most common neurologic signs and symptoms associated with lesions of this structure.

**MLF CIRCUITRY OF SACCADIC EYE MOVEMENTS** The saccadic apparatus includes neurons in the frontal eye field (FEF) which project to a number of subcortical structures that serve to mediate rapid gaze shifts to remembered targets. The FEF sends a signal to the ipsilateral superior colliculus (SC) and to the contralateral paramedian pontine reticular formation (PPRF) for horizontal saccades and to the rostral interstitial nucleus of the MLF (rMLF) for vertical saccades. The PPRF contains excitatory burst neurons that produce the supranuclear horizontal saccadic eye velocity command sequence (the pulse). These neurons project to the adjacent VI (abducens) nerve nucleus. The abducens nucleus consists of two types of neurons that mediate conjugate horizontal eye movements. Abducens motoneurons innervate the ipsilateral lateral rectus muscle whereas axons from abducens interneurons cross to the contralateral pons and ascend via the MLF to innervate the medial rectus subnucleus of cranial nerve III, which ultimately projects to the medial rectus muscle (figure 1). The parietal cortex is central in the production of smooth pursuit eye movements but also participates in the production of saccades and has a direct projection to the SC. In contrast to the FEF, the parietal cortex is more involved in the production of saccades to novel visual stimuli rather than to remembered targets. As with saccades, smooth pursuit pathways ultimately converge upon the MLF for the execution of both horizontal and vertical eye movements.

**VESTIBULAR COMPONENTS OF THE MLF CANAL SYSTEM AFFERENTS.** The MLF is the principal tract system by which signals reach the ocular motoneurons for eye movements generated in response to vestibular stimuli. There may, however, be differences in the anatomic circuitry underlying these reflexes depending upon whether the eye movements are compensatory for angular motion of the head mediated by the semicircular canals (called the rotational vestibular ocular reflex; r-VOR), or for linear acceleration of the head, mediated by the otolith organs (utricle and saccule).

**LATERAL SEMICIRCULAR CANAL PROJECTIONS IN THE MLF.** The pathways underlying the angular VOR are reasonably well understood. For the lateral canal system, the r-VOR is mediated by the same pathway carrying information for the other conjugate eye movement systems (saccade and pursuit). The abducens nucleus is the gaze center for the final pathway of horizontal eye movements. Stimulation of the lateral semicircular canal results in transmission of information (from horizontal head motion or caloric activation) within the ipsilateral VIII nerve and nucleus. Projections then emanate from the medial vestibular nucleus to innervate the contralateral VI nucleus.
Motoneurons then project to the lateral rectus muscle, while abducens interneurons project into the contralateral MLF where their axons innervate the medial rectus subnucleus of the ocular motor nucleus with a final projection to the medial rectus muscle (figure 2).

Anterior semicircular canal projections in the MLF. For the anterior canal system, there may be three excitatory pathways by which information is carried rostrally for the vertical r-VOR. Excitatory cells in the medial vestibular nucleus or adjacent ventral lateral vestibular nucleus (VLVN) project medially and dorsally, crossing the midline caudally. After crossing, they ascend in or just below the MLF to contact the superior rectus and inferior oblique subdivisions of the oculomotor complex. Importantly, the superior rectus subnucleus sends fibers that decussate to innervate the superior rectus muscle on the side of anterior canal activation (figure 3). In this way, one semicircular canal can innervate muscles in both eyes for appropriate yoking of eye movements. Inhibitory neurons for the anterior canal system lie in the superior vestibular nucleus (SVN). Their axons exit from the rostromedial aspect of this nucleus and course medially and rostrally in the lateral wing of the ipsilateral MLF, to contact superior oblique motoneurons in the trochlear nucleus, and superior rectus neurons in the oculomotor nucleus, to antagonize those eye movements mediated by an activated anterior canal system.

Another cell group that may contribute excitatory inputs from the anterior canal system lies in the SVN. Their axons cross the midline in the ventral tegmental tract, close to the medial lemniscus at the rostral pole of the nucleus reticularis tegmenti pontis (NRT-P), and then abruptly turn rostrally, passing through the decussation of the superior cerebellar peduncle, to terminate mainly on the superior rectus and inferior oblique subdivisions of the oculomotor complex. Also, in some species (perhaps also in humans), the SVN projects rostrally, just near the brachium conjunc-
Axons from the canal project to the ipsilateral vestibular nuclei, and then decussate to innervate the contralateral inferior rectus subnucleus of the oculomotor complex of cranial nerve III and the trochlear nucleus. The trochlear neurons then exit the brainstem posteriorly and decussate back to the left side innervating the superior oblique muscle. Activation of both canals (as with pitching the head upward and attempting straight ahead fixation) will result in cancellation of the torsional vector components, but addition of the vertical vector components resulting in downward movement of the eyes.

Posterior semicircular canal projections in the MLF. For the posterior canal system, excitatory neurons project from the vestibular nuclei at the junction of the MVN and VLVN rostrally, medially, and dorsally through MVN until, at the level of the caudal abducens nucleus, they turn medially and cross the midline beneath the nucleus prepositus hypoglossi (NPH) and abducens nucleus, ventral to the MLF. After crossing the midline, they enter the MLF and project rostrally to the trochlear nucleus and inferior rectus subdivision of the oculomotor complex. The trochlear axons within cranial nerve IV then exit the brainstem posteriorly (the only cranial nerve to do so) and completely decussate before projecting forward to innervate the superior oblique muscle (on the side of posterior canal activation) (figure 4). Inhibitory neurons subserving the posterior semicircular canals are found in the SVN and rostral MVN. Their axons project through the pontine reticular formation to reach the ipsilateral MLF and then contact the superior rectus and inferior oblique subdivisions of the oculomotor complex in order to avoid movements antagonistic to those mediated by the posterior canal system.

An important clinical implication of the difference in anatomic projections of the posterior and anterior canal pathways is that patients with MLF lesions may have a dissociated vertical nystagmus and relative sparing of response to upward vs downward rotation of the head.

Otolithic projections in the MLF. The otolith organs detect linear acceleration. The projections from the vestibular nuclei that mediate otolith-ocular reflexes are less well defined and there is a paucity of evidence for a direct three neuron arc (e.g., otolith organ, vestibular nucleus, ocular motor neuron) comparable to the three neuron arc for semicircular canal mediated reflexes. Presumably the horizontal translational VOR is mediated by the same abducens nucleus pathway as are the other conjugate systems, though there is some evidence for a direct projection of utricular afferents to the abducens nucleus.

Responses to static head tilt, especially lateral tilt of the head (ear to shoulder), have been long known to produce ocular counterrolling, due to activation of the cyclovertical ocular muscles. Under normal circumstances, when the head is tilted to the left, the eyes counterroll in the opposite direction (upper poles of the eyes slowly moving away from the side of the tilt). This reflex is mediated by projections that innervate the left eye intortors (superior rectus and superior oblique) and the right eye extortors (inferior rectus and inferior oblique) (figure 5). Following the slow phase counterroll, there is a fast torsional movement in the opposite direction (upper poles beating to the side of the head tilt) which is mediated by the riMLF in the rostral midbrain.

Anatomically, these graviceptive pathways cross to the other side of the brainstem approximately in the middle of the pons and further ascend in the MLF to the ocular motor nuclei (nuclei III and IV) and the premotor gaze centers in the rostral midbrain (interstitial nucleus of Cajal [INC] and riMLF). From there, further connections reach multiple cortical areas through thalamic projections.

A common clinical finding in patients with unilateral MLF lesions involving the central otolith pathway is the ocular tilt reaction (OTR), which consists of a head tilt, ocular counter-rolling [generally with the upper pole of the eyes
In this example, a left head tilt results in a counterclockwise (with respect to the examiner) torsional counterroll of the upper poles of the eyes. This response is mediated by a crossed otothl projection to the extorters in the patient’s right eye (the inferior oblique and inferior rectus muscles) and a double crossed projection to the intorters of the left eye (the superior oblique and superior rectus muscles). These slow phases are punctuated by torsional fast phases that are mediated by the rostral interstitial nucleus of the medial longitudinal fasciculus. The interstitial nucleus of Cajal (INC) is also shown (without connections). This important midbrain structure contains circuitry important for neural integration of vertical and torsional gaze, eye-head coordination during roll movements, and contains inhibitory burst neurons for vertical eye movements. Lesions of these otothl projections result in the opposite reciprocal effects leading to intorsion and elevation of the right eye and extorsion and depression of the left eye, the so-called skew deviation. If the lesion occurs prior to the otolith pathway deussation (here on the left) then the lower left eye is on the side of the lesion. Alternatively, if the lesion is within this pathway after the deussation (in the pons or midbrain), then the higher eye is on the side of the lesion. Rotating toward a lesion below the pons and away from a lesion at the level of the pons or midbrain, and skew deviation (a supranuclear vertical misalignment of the two eyes). The head tilt is typically away from the side of the higher eye.

In typical skew deviations, the higher eye is contralateral to a medullary lesion and ipsilateral to a mid pontine (the level at which otothl projections deussate the brainstem) or midbrain lesion. Ocular counterroll may be recognized during funduscopic examination, where the horizontal plane between the optic disc and macula (the macula-disc line) is now deviated. For example, in the case of a left lateral medullary syndrome, an ocular tilt reaction might involve left head tilt, right hyperdeviation, and counterroll of the eyes (upper poles) toward the left shoulder (or clockwise rotation with respect to the observer). In essence, the macula of the left eye is now further below the disc than usual, and the macula of the right eye is further above the disc (figure 6).

Tilting the head relative to gravity from upright in an ear-down direction, so called head roll, elicits dissociated changes of eye position. In healthy subjects, both eyes counterroll (upper poles of the eyes moving away from the side of the head tilt) by roughly 10% of the head roll, but the extorting eye rotates about 1 to 2 deg more than the intorting eye (figure 5). Furthermore, a small skew deviation (vertical misalignment) of about 0.5 deg appears with hypertropia of the intorting eye. Unilateral peripheral or pontomedullary lesions below the pontine crossing of the graviceptive pathways produce a skew deviation and binocular torsion (combination of these signs is sometimes called skew torsion). For instance, a patient with a left medullary lesion will have a right hypertropia and counterroll of the eyes toward the left shoulder (figure 7). Lesions of the lower graviceptive pathways tend to produce disconjunctive torsion, which is typically greatest in the excyclotorted eye. In contrast, a unilateral pontomesencephalic brainstem lesion leads to contraversive skew torsion. In this case, the hypertropic eye is ipsilateral to the lesion and the ocular torsion is usually conjugate and to the shoulder opposite the side of the lesion. If skew torsion is associated with a head tilt in the direction of the lower eye, this configuration of clinical signs is called ocular tilt reaction. Since both graviceptive pathways and internuclear connections between ocular motor nuclei travel along the MLF, skew torsion due to pontomesencephalic lesions is frequently associated with internuclear ophthalmoplegia (INO) (see INO section). The hypertropic eye is generally on the side of the INO (figure 8).

**INTERNUCLEAR OPTHALMOPARESIS** The most commonly recognized syndrome that results from MLF damage is INO and is characterized by slowing or limitation of adduction (on the same side as the MLF lesion) during horizontal eye movements (figures 8 and 9).

In patients with INO the contralateral abducting eye will usually exhibit a disassociated horizontal nystagmus, although this does not always occur. One hypothesis to explain abduct nystagmus implicates an adaptive response to overcome the weakness of the
The lesion was at the level of the left midbrain (after the decussation of the rightward originating otoith pathways) and involved the medial longitudinal fasciculus. Also note the enlarged left pupil, which exhibited the characteristics of near-light dissociation.
Volitional saccadic pathway with a lesion in the right MLF that results in an INO during an attempted saccade to the patient’s left.

**INO+ SYNDROMES** One-and-a-half syndrome. This syndrome consists of a gaze palsy in one direction with an INO when executing a saccade to the opposite side. It is produced by damage to the PPRF or abducens nucleus and the MLF on the same side within the pontine tegmentum. Convergence is generally spared as cranial nerve III is spared bilaterally. Given the preserved abduction of the eye contralateral to the lesion, one commonly observes a primary position exotropia also known as paralytic pontine exotropia (figure 11).

Wall-eyed bilateral INO syndrome. If the lesion affects the MLF within the pons or midbrain, vergence pathways and the oculomotor apparatus can be coincidentally disrupted, resulting in a variety of eye movement abnormalities that include impaired convergence. These lesions are typically bilateral and produce divergence of the eyes (wall-eyed) (figure 12).

INO and trochlear syndrome. A highly unusual syndrome involves a unilateral lesion of the MLF at the level of the caudal midbrain with extension into the trochlear nucleus on the same side.

This lesion produces an INO and contralateral hyperdeviation secondary to a IV nerve palsy (remember the trochlear nerve exits and decussates to innervate the opposite side superior oblique muscle). This syndrome can be confused with a
skew deviation; however, in the case of INO and skew deviation, the hyperdeviation is generally on the side of the INO.

ABNORMAL VERTICAL EYE MOVEMENTS WITH MLF LESIONS The MLF contains pathways involved in the regulation of vertical pursuit, vertical vestibular signals, and vertical alignment. Patients with INO will therefore often exhibit abnormalities with vertical eye movements, including the following: diminished vertical gaze holding, abnormal optokinetic and pursuit responses, decreased vertical VOR gain, vertical gaze-evoked nystagmus, convergent-retraction nystagmus, decreased vertical smooth pursuit, and skew deviation.

CLINICAL MANIFESTATIONS OF INO The clinical manifestations associated with INO include diplopia (typically horizontal binocular), visual confusion, the illusion of environmental movement during horizontal saccades (oscillopsia), vertigo, and blurring of visual image acuity, particularly with reading. A less conspicuous, but potentially dangerous feature includes worsening disconjugacy and a resultant break in binocular fusion during head active turning (which produces a contraversive slow phase punctuated by saccades in the direction of head movement), while head turning during driving (e.g., changing lanes), and while ambulating.

RADIOGRAPHIC IDENTIFICATION OF MLF LESIONS Several pathologic studies have shown a clear anatomic relationship between the presence of lesions along the ipsilateral MLF and the presence of INO. Due to its high spatial resolution, MRI has allowed us to depict in vivo the anatomic organization of the human oculomotor nerve complex, the MLF, and related structures in the brainstem (typically white matter tracts have low signal intensity and nuclei have higher signal intensity). Moreover, MRI has also contributed to a better understanding of the different stages of myelination of these structures in the preterm brain.

In patients with INO, MRI has shown hyperintense lesions in the region of the MLF on T2-weighted images that were not detected using CT. T2-hyperintensities in the pontine and midbrain tegmentum portion of the MLF have been shown in a high percentage of patients with INO derived from different neurologic disorders (figure 13). In one study involving 58 patients with MS, with INO, MRI with proton density imaging detected a higher percentage of MLF involvement (100%) than T2 (58%) and fast-FLAIR (48%).

We have recently studied the relationship between the severity of INO and corresponding measures of brain tissue injury within the MLF, derived from the advanced neuroradiologic techniques diffusion tensor imaging and magnetization transfer imaging. The application of neurophysiologic methods in the quantitative

Figure 11 An example of the one-and-a-half syndrome in one of our patients with multiple sclerosis.

The patient was unable to elicit saccades to the right (i.e., a right gaze palsy), and had evidence of a right internuclear ophthalmoparesis (INO) upon attempted gaze to the left. In this photograph, the patient is looking straight ahead. We can observe an exotropia, the so-called paralytic pontine exotropia with the left eye in exo (the only remaining movement possible). In this circumstance, there is an attempted leftward preference. However, only left eye abduction is possible given the right INO (with slowing and significant ocular limitation). Below is the T2-weighted axial MRI showing the responsible lesion involving the right pontine tegmentum (arrow).

Figure 12 The syndrome of wall-eyed bilateral internuclear ophthalmoparesis (INO) in a patient with multiple sclerosis with progressive disease and a history of a severe inflammatory demyelinating syndrome involving the tegmentum of the pontomesencephalic junction, which affected the medial longitudinal fasciculus (MLF) bilaterally.

Note the exotropic appearance of both eyes (i.e., wall-eyed). Attempted gaze to the right or left revealed adduction slowing and limitation consistent with bilateral INO. There was also reduced vertical smooth pursuit and vertical vestibulococular reflexes (both pathways course through the MLF).
analysis of a clinically discrete syndrome, and the characterization of its corresponding neuroradiologic measures of tissue injury, provide a strategy for studying the relationship between clinical disability and the spectrum of brain tissue histopathology in MS.

Two structures responsible for the generation and gaze stability of vertical and torsional eye movements, the rMLF and the INC, are located in the mesencephalon. In 11 patients with MRI-identified mesencephalic lesions and clinical evidence of torsional/vertical spontaneous nystagmus, Helmchen and colleagues showed that combined lesions of rMLF and INC are much more frequent than rMLF and INC lesions alone.39

More recently, modern MR-based techniques have been used to achieve a better in vivo picture of the underlying pathologic changes of many neurologic conditions. Diffusion tensor MRI can identify infarctions involving the MLF and also reveals detailed information regarding white matter fibers tract anatomy and direction.40 Using line scan diffusion MRI, Mamata and colleagues visualized, in six healthy volunteers, the principal fiber tracts of white matter, including the MLF.41

### DISEASES TARGETING THE MLF Cerebrovascular disease. The most common cause of INO in an older patient is ischemic infarction. These patients are typically older than patients with MS, with an average age of 62–66 years.42 In contrast to MS, most (87 to 93%) INO syndromes in this setting are unilateral. In a large case series of 410 cases of INO evaluated by the same observer, stroke was the most common cause of INO (38%).42 In this series, individual cases of INO are reported with varied stroke subtypes, including hemorrhage (hypertensive, vascular malformation), vertebral artery dissection, temporal arteritis, and other vasculitides.

### Multiple sclerosis. MS constitutes the second most common cause of INO, representing approximately one-third of cases (34%), and is the most common cause in a young person (<45 years), where most are bilateral.42

Inflammation in MS is contingent upon trafficking of mononuclear cells across the cerebrovascular endothelium in a process mediated by well-characterized adhesion molecules. Postcapillary venules provide the scaffolding for adhesion and trafficking into the CNS and have their greatest concentration in areas around the periventricular zones.43,44 As such, the brainstem tegmentum is an area of high predilection for disease activity in MS.

### Other etiologies. A large number of causes make up the one-quarter to one-third of INO cases that are not due to MS or cerebrovascular disease (table). The most common of these are infection, trauma, and tumor. In some remarkable examples, mild head injury can produce an isolated unilateral or bilateral INO.55,46 A partial third nerve palsy with prominent medial rectus weakness may be confused with an INO. Distinguishing features include other third nerve deficits (weakness of elevation, ptosis, pupil dilation), im-

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**Figure 13** A highly conspicuous lesion in the midbrain tegmentum just ventral to the cerebral aqueduct (left image, arrow) and a highly characteristic lesion in the MLF of the pontomesencephalic junction (right image, arrow) (3 mm thick, axial proton density weighted sequences) was noted.

Both images were derived from patients with multiple sclerosis and bilateral internuclear ophthalmoparesis. Both lesions demonstrate the eloquence principal of periventricular demyelinating lesions that are localized to the brainstem, in contrast to the non-eloquence of many cerebral periventricular lesions (that often do not correspond to any concomitant clinical manifestations).
paired convergence, and absence of the contralateral abduction nystagmus, all of which point to a third nerve palsy rather than an INO.

Eye movement abnormalities including INO have been reported in progressive supranuclear palsy (PSP). Parkinsonism and other features of PSP are present in these individuals, and most eye movement abnormality can be overcome with oculocephalic maneuvers (confirming its supranuclear character), but not in an INO (confirming its nuclear character).

A pseudo-INO is a well-described phenomenon in patients with myasthenia gravis and Guillain-Barré syndrome. The presence of ptosis and lid fatigue will alert the clinician to myasthenia, while areflexia, usually with ataxia or limb weakness, will suggest Guillain-Barré syndrome. The Miller-Fisher syndrome involves ocular motor dysfunction (potentially with INO), ataxia, and diminished or absent reflexes. Findings suggestive of bilateral INO have also been reported in the setting of drug overdose; however, these individuals would be expected to have severely impaired level of consciousness.

PROGNOSIS AND TREATMENT The deficits associated with INO often resolve over a few weeks to months. In one series, patients with a cerebrovascular etiology were less likely to recover; 63% had persistent symptoms after 3 years. Others have observed a better prognosis with INO due to brainstem infarction, with 79 to 87% recovery in 2 to 3 months.

Patients may be treated with patching of one eye for symptomatic relief. Patching of the affected eye may be helpful for those persons who experience diplopia as a result of their INO. When the syndrome is secondary to MS, corticosteroids can serve to accelerate recovery, albeit limited in many. Since most patients are well aligned in primary position of gaze (with good binocular fusion), and the double vision is typically provoked in eccentric gaze, the use of prisms is usually not helpful. However, a concomitant and stable skew deviation may be amenable to prismatic correction to abolish the vertical misalignment (and consequent diplopia) of the eyes.

RECENT ADVANCES AND FUTURE DIRECTIONS INO is one MLF-related syndrome that represents a useful model by which to objectively characterize a distinctive neurologic syndrome and its corresponding disability, with associated imaging measures of brain tissue injury. This strategy may represent a useful proof of principle model of pathophysiology upon which to test neuroprotective and neurorestorative therapies such as promoters of axonal sprouting and stem cell remyelination initiatives. This is of particular interest given the periventricular location of the MLF and that stem cells may be effectively delivered into the ventricular system.

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REFERENCES
INTERNATIONAL ISSUES

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

The Krakow experience

In the heart of Krakow sits the Klinika Neurologiczna. As part of the School of Medicine of Jagiellonian University in Poland, this building serves as a center for the care of patients with neurologic diseases and as a facility to train medical students. Within the Klinika is Babinski Hall. Named for the renowned Polish neurologist Dr. Joseph Babinski (1857–1932), this lecture hall provides students with a location to learn from their peers, instructors, and patients. Within a short walk of Babinski Hall are several reminders of the city's rich history. Wawel Castle sits on a hill overlooking the Wisła River, nestled closely against one of Poland's national cathedrals. Giant bones reported to be those of the city's ancient dragon lie anchored to the cathedral with metal shackles. Legend claims that as long as these bones exist, so will the cathedral.

Jagiellonian University, established in 1634, is the second oldest University in central Europe. Copernicus trained there, as did Pope John Paul II before he became Pope. The historic St. Mary's Basilica still towers over the famous Rynek Główny, one of the largest marketplace squares in Europe. On a typical day, the square is packed with tourists, businessmen, and locals. Some saunter across the stone pavement, while others relax over a meal and drink. St. Mary’s Basilica provides a unique musical experience for those nearby. On the hour, every hour, a lone trumpeter plays an unfinished tune (the hejnal) from each of the four corners of the Basilica's highest tower. The tune is always stopped abruptly at the same point to commemorate the original trumpeter who took an arrow in the throat while attempting to warn the town of a pending Mongol attack.

In the spring of 2005, Dr. David Gill, Dr. Ralph Jóźefowicz, and I were invited to Krakow to help instruct and train students at the Jagiellonian University School of Medicine. This opportunity, originally developed through Dr. Jóźefowicz’s efforts, is offered once a year to University of Rochester chief neurology residents and is funded by both universities. At the time, I was a father of a 3 month old and considered declining the offer because of the added complications of traveling with a young child. In the end, I accepted the offer, and I have never regretted my decision.

Babinski Hall is different from most American lecture halls. On one side of the steep auditorium, a wall of windows. In the spring months, these windows provide a pleasant view of blossoming maple trees from the clinic's courtyard. Within the hall, students take notes behind a series of long wooden desks. The acoustics and layout are excellent. A lecture can be seen and heard from any point on the presenting stage without the use of a microphone. An old sign with Babinski’s name hangs over the main entrance. In direct contrast to the aged wooden desks, the room has been modified and modernized with a video projector and laptop computer to assist with didactic presentations.

Some of the medical students at Jagiellonian University have spent their entire lives in Poland, whereas others transferred in from other countries to learn medicine. Despite being a Polish school, all classes are taught in English. On the whole, the students are diligent, bright, conscientious and show a high degree of collegiality.

The Polish medical student’s involvement in patient care is different than in the United States. During my own medical school training, I often found myself rounding on, writing notes for, and prescribing medication for more than 10 patients at a time (although admittedly this number seems to get larger the further I get away from my own medical school training). At the Klinika, medical students typically do not write notes in patients’ charts and often do not round with the primary resident and attending team that is directly taking care of the patients. As students, they are allowed to examine patients and take histories but often are not present during many management discus-

Disclosure: The author reports no conflicts of interest.
visions. As an alternative way of education, students are expected to learn from their patients via attending teaching conferences. During these conferences, medical students are asked to consent and bring their patients directly to Babinski Hall.

In Babinski Hall, students present a patient's medical history to their teaching attending and to the rest of their class. As the teaching physician, I enjoyed this experience. I would introduce myself to the patient and then obtain a history through a Polish interpreter. At the completion of the interview, I would perform a complete neurologic examination for the students while pointing out critical examination features. After discussions with the patient and the class, each volunteer was taken back to his or her own hospital bed. In addition, each primary medical team would be notified of the insights provided by the evaluation.

The neurologic cases were similar to what we see in the United States. While there, I examined patients with multiple sclerosis, seizures, stroke, and encephalopathy. In a more unusual case, I identified pyridoxine toxicity in a young woman who presented with a sensory neuropathy.

Initially, I thought that many Polish patients would refuse to participate in the "teaching theater" because of the degree of exposure that it required. Not only did patients participate, but they often expressed their gratitude for the added insight into their disease and for being able to assist in student education. In cases in which a patient was too ill to leave his or her bed, I would implement traditional bedside teaching with smaller groups. Both methods of teaching were equally well received by the students.

While in Poland, I also had the opportunity to lead neurology case discussion groups and give four 1-hour didactic lectures on the topics of primary brain neoplasm, status epilepticus, cerebral infarction management, and subarachnoid hemorrhage. During the medical students' neurology rotation, they received two to three didactic lectures a day, followed by patient and small group discussions.

Despite cultural and language differences, it was relatively easy to teach neurology in Poland. As a focus of my own residency, I had previously instructed medical students, given case presentations during neurology grand rounds, and given neuromuscular lectures to our faculty. I found that this background prepared me well to teach the Krakow students.

Clinically, the limitations in accessing select imaging studies and tests were easily compensated for by relying on neurologic fundamentals: a good history, a thorough examination, and a logical thought process. These fundamentals re-
main essential in the art of neurology, irrespective of the country in which a physician practices.

Overall, my international teaching experience was invaluable. The time spent evaluating Polish patients and training Polish medical students helped me garner a greater appreciation for international neurology. After one month, I felt that I had improved my skills as a neurologist. Specifically, during that time, I was able to focus on my clinical history and neurologic examination skills in isolation from an abundance of ancillary testing.

Since returning from Krakow, I have found that I rely more on clinical fundamentals and less on ancillary testing. Practicing and teaching neurology in Krakow not only helped sharpen my clinical skills and teaching techniques but also gave me a greater appreciation of the global efforts against neurologic disease. The international neurology experience may be one of the better ways to personally experience these benefits. It is likely that even Joseph Babinski would have agreed.

### 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 2500 words; permission for longer articles will be needed from the editors. The number of references should be ten or less and 1-2 tables or figures can 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 have the same requirements as NeuroImages but are especially valuable to the trainee audience and will be published in the online Resident and Fellow Section. A number of new categories were added in 2007. Queries and comments should be addressed to Mitchell Elkind, MD, MS, FAAN, or Kathy Pieper at kpieper@neurology.org.
EDUCATION RESEARCH AND INITIATIVES

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:
Evaluating acute altered mental status
Are incoming interns prepared?

ABSTRACT
Background: Clinical evaluation of hospitalized patients with acute altered mental status (AMS) is a common task of interns, regardless of medical specialty. The effectiveness of medical education to ensure competence in this area is unknown.

Objective: To measure competency of new interns in the evaluation and management of AMS using an Objective Structured Clinical Examination (OSCE).

Methods: A cohort study was conducted with 61 medical school graduates entering internship at a single teaching hospital in 2006. Interns from all major specialty fields were included. The OSCE consisted of a 12-minute simulated encounter with a human patient simulator and nurse actor. Each intern’s performance was graded by the same neurologist, using criteria agreed upon by consensus of the neurology faculty. Competency in obtaining a history, performing a neurologic examination, generating a differential diagnosis, and ordering diagnostic studies was graded. Overall performance was scored on a percentage scale from 0 to 100.

Results: Overall performance scores ranged from 19 to 43 with a mean of 31.4 (SD ± 5.6). Hypoglycemia was identified as a potential cause of AMS by 72.1% of interns, while fewer identified urinary tract infection (45.9%) and seizure (13.1%). While many interns ordered a CXR (86.9%) and head CT (80.3%), few requested a toxicology screen (21.3%) or lumbar puncture (3.3%). Only 41% of interns performed a neurologic examination.

Conclusion: New interns are not well-prepared to evaluate patients with altered mental status in the inpatient setting as measured by an Objective Structured Clinical Examination. Neurology® 2008;71:e50-e53

GLOSSARY
AMS = altered mental status; OSCE = Objective Structured Clinical Examination.

Altered mental status (AMS) is a general term used to describe the undifferentiated presentation of a group of disorders affecting cognitive function or alterations of consciousness. Approximately 5–10% of patients presenting to the emergency department have AMS,¹ and an estimated 10–50% of hospitalized patients will experience acute AMS, or delirium.² Clinical evaluation of patients with acute AMS is a common task encountered by the intern on call, regardless of medical specialty. The effectiveness of medical education to ensure competence in this area is unknown.

The Objective Structured Clinical Examination (OSCE) is being increasingly used in medical schools and postgraduate training programs across the United States and Canada. The OSCE provides a standardized means of assessing skills in obtaining a history and performing a physical examination, communicating with patients and members of the health care team, formulating a differential diagnosis, and developing a management plan.³ An OSCE most often uses standardized patients as the primary assessment tool; however, other simulation tools may be utilized, including data interpretation, technical skills stations (e.g., suturing

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practicum), and clinical scenarios with human patient simulators (i.e., programmable mannequins). The advantages to simulations are that they incorporate a wide array of options for diagnosis, allow the examinee to reason through the problem with little or no cueing, permit participants to make life-threatening mistakes with no danger to real patients, and provide opportunity to take corrective action.2

The purpose of this study was to measure the competency of new interns in the evaluation and management of acute AMS using a clinical scenario with a human patient simulator as part of an OSCE. We also sought to correlate performance with surgical vs nonsurgical specialties, and with prior neurologic clerkship exposure.

**METHODS** A cohort study was conducted with 61 medical school graduates entering internship at a single military teaching hospital in 2006. Interns from 10 specialty fields were included (Table 1). There were 43 allopathic and 18 osteopathic physicians in the group, matriculating from 39 different US medical schools. The AMS station was one of eight stations utilized as part of an OSCE to assess competency in a variety of areas pre-internship. The combined data of the eight-station OSCE will be presented elsewhere. The AMS OSCE consisted of a 12-minute encounter with a human patient simulator (computer-programmed mannequin) and a nurse actor (the examiner). Each intern’s performance was graded by the same neurologist, using a modified checklist with criteria agreed upon by consensus of the neurology faculty. Competency in obtaining a history, performing a neurologic examination, generating a differential diagnosis, and ordering diagnostic studies was graded. Elements in the areas of patient care and medical knowledge were scored as “performed” or “not performed.” Elements in the areas of interpersonal communication skills and professionalism were scored using a five-point Likert scale from “poor” to “excellent.” Overall performance scores were converted to a percentage scale from 0 to 100. Scores were compared between surgical and nonsurgical specialties, and for those with neurology clerkship experience vs prior experience using an unpaired Student t test.

Each intern was given the clinical scenario by the nurse actor and allowed 8 minutes to examine the human patient simulator, which was programmed with heart sounds, pulses, breath sounds, and blood pressure. A stethoscope, penlight, and reflex hammer were provided. The clinical scenario was read as follows: “There you are, Doctor. I just paged you to come take a look at Mrs. Gray. My name is Ms. ______ one of the nurses on this general medicine ward. I know you are covering call and normally don’t follow Ms. Gray, but she is not acting like herself and I need you to evaluate her and tell me what needs to be done. She appears somewhat agitated, her arousal waxes and wanes, she seems confused, she is difficult to understand, and does not answer questions appropriately. Since she is not responding well to questions, I can give you some additional history from what I know since starting this shift.”

The interns were allowed to ask questions of the nurse, verbalize their diagnostic considerations, order diagnostic tests and consultations, and request treatments to be administered. At the completion of 8 minutes, each intern was given an additional four minutes to write their responses to the following questions: 1) List the possible causes of altered mental status in any patient. 2) What laboratory studies would you consider in a patient with altered mental status? 3) What other diagnostic tests would you consider in a patient with altered mental status? 4) What is the treatment plan for this patient? The examiner positively scored any item given by the examinee in verbal or written form.

**RESULTS** Sixty-one interns were evaluated on a total of 103 items divided into the following Accreditation Council for Graduate Medical Education core competency categories: medical knowledge (27 items), patient care (55 items), interpersonal communication skills and professionalism (8 items), and systems based practice (3 items). The overall performance score ranged from 19 to 43, with a mean of 31.4 (SD ± 5.6). There was no significant difference between surgical and nonsurgical interns or between those interns with or without previous neurology exposure (Table 2).

In the combined areas of interpersonal communication skills and professionalism, the mean raw score was 21.2 ± 7.03 (from a possible 40 total points) or 52.9% ± 17.6. There was no significant difference between surgical (n = 25) and nonsurgical interns (n = 36) with respect to these scores, or between those who had prior neurologic clerkship exposure (n = 44) and those who did not (n = 17) (Table 2).

The mean subset scores were 25.2 ± 6.1 in medical knowledge and 38.4 ± 6.8 in patient care. Most interns performed a heart and lung examination (96.7%), but only 41% performed a neurologic examination of any kind. A total of 80.3% of interns requested vitals signs, and 67.2% requested any past

<table>
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<tr>
<th>Specialty fields of the interns and overall performance scores</th>
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<tr>
<td>Medical specialty (n) Overall performance score (average)</td>
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<tr>
<td>Family medicine 8 31.0</td>
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<tr>
<td>Emergency medicine 8 31.8</td>
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<tr>
<td>General surgery 5 30.5</td>
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<tr>
<td>Internal medicine 10 34.3</td>
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<tr>
<td>Neurology 3 31.0</td>
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<tr>
<td>Obstetrics-gynecology 4 32.9</td>
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<tr>
<td>Otolaryngology 2 25.9</td>
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<tr>
<td>Pediatrics 8 30.8</td>
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<tr>
<td>Orthopedics 3 30.2</td>
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<td>Transitional year 10 31.1</td>
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medical history. The most common etiologies (table 3) given for altered mental status were hypoglycemia (72.1%), sepsis (65.6%), and hypoxia (60.6%). Less commonly identified etiologies were alcohol intoxication/withdrawal (36.1%), seizure (13.1%), meningitis/encephalitis (11.4%), and hypo/hypernatremia (9.8%). While many interns ordered a chest x-ray (86.9%) and head CT (80.3%), few requested a toxicology screen (21.3%) or lumbar puncture (3.3%). More striking, only 4.9% (3/61) of interns called their supervising resident or attending, even when planning to transfer the patient to a higher level of care. This particular result may be falsely low, however, taking into consideration the artificial nature of the OSCE.

**DISCUSSION** This study measured the competency of incoming interns to clinically evaluate a patient with acute AMS using an OSCE. AMS may occur in 14–56% of hospitalized patients at a cost of about $4 billion annually. Identification of risk factors and a systematic approach to management can improve the outcome of the syndrome. We found that incoming interns performed quite well in certain areas and quite poorly in others, particularly in formulating differential diagnoses pertinent to neurologic disease or diagnostic evaluations specific for neurologic disease.

Acute AMS with alterations in arousal, or delirium, is associated with high mortality and morbidity in older hospitalized patients and indicates severe illness in younger patients. Some of the most common causes of acute AMS presenting to the emergency department include neurologic (28%, including stroke, intracranial hemorrhage, and seizure), toxicologic (21%, including alcohol, illicit drugs, and medication adverse effects), infectious (10%), and...

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<th>Table 2</th>
<th>Intern specialties and neurology exposure</th>
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<tr>
<td></td>
<td>All Interns</td>
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<tr>
<td>No. of interns</td>
<td>61</td>
</tr>
<tr>
<td>Mean overall performance score (percentage)</td>
<td>31.4 ± 5.6</td>
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<tr>
<td>Mean subset score</td>
<td></td>
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<tr>
<td>Patient care</td>
<td>38.4 ± 6.8</td>
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<tr>
<td>Medical knowledge</td>
<td>25.2 ± 6.1</td>
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<td>Professionalism and interpersonal skills</td>
<td>53.2 ± 17.6</td>
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<tr>
<td>Prior neurology exposure</td>
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<th>Table 3</th>
<th>The most common etiologies given for altered mental status</th>
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<tr>
<td>Etiology</td>
<td>Interns identifying as potential etiology of AMS (%)</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>72.1</td>
</tr>
<tr>
<td>Sepsis</td>
<td>65.6</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>62.3</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>60.6</td>
</tr>
<tr>
<td>Medication effects</td>
<td>49.2</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>47.5</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>45.9</td>
</tr>
<tr>
<td>Alcohol intoxication/withdrawal</td>
<td>36.1</td>
</tr>
<tr>
<td>Seizure</td>
<td>13.1</td>
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<tr>
<td>Meningitis/encephalitis</td>
<td>11.4</td>
</tr>
<tr>
<td>Hyper/hyponatremia</td>
<td>9.8</td>
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metabolic (5%). Among hospitalized elderly patients with AMS, common etiologies are drug toxicity (56%), acute cardiovascular disease (48%), acute metabolic disturbances (43%), and neurologic disease (37%).

The results of this study raise some concern about the preparedness of new interns. Fewer than half of the interns tested recognized common neurologic etiologies, including intracranial hemorrhage or seizure as a cause of AMS, despite neurologic causes accounting for approximately one-third of all cases of AMS. Medication toxicity accounts for approximately 20–50% of acute delirium, depending on the study population, yet this was identified by only about half of the cohort. It is also important to note that only 41% of the interns tested even performed a neurologic examination.

The OSCE has been increasingly used over the past several years in both undergraduate and graduate medical education facilities to test a variety of skills, including cardiac physical examination skills with live patients and human patient simulators, competency in performing the neurologic examination, and clinical skills mastery in obstetrics and gynecology during medical clerkships.

There are several limitations to this study. The study sample was small and was limited to one incoming class of interns at a single teaching hospital. Although the interns evaluated in the study were all graduates of US medical schools, the findings may not be representative of all medical schools or teaching hospitals. Additionally, performance on the OSCE, which is an artificial time-limited scenario, may not fully reflect performance in real situations. It may be that overall percentile scores were lower due to the large number of items on the scoring form and the inherent time limitation of the OSCE. Finally, the absence of published practice guidelines for AMS necessitated that we establish our own performance standards based on faculty consensus.

The results of this study suggest opportunities for improving the training and education of medical students and interns. Further studies are needed to compare pre- and post-internship competency, impact of participation in a neurology rotation during internship, and teaching modules specifically designed for the evaluation of AMS in the hospital setting.

Received March 7, 2008. Accepted in final form July 22, 2008.

REFERENCES
TEACHING NEUROIMAGES

Teaching *NeuroImages* are interesting, previously unpublished photomicrographs, patient photographs, neuroradiologic images, or other pictorial material. They should be particularly clear examples of established observations intended for the trainee audience.
A 57-year-old man with cerebrotendinous xanthomatosis (CTX) was admitted to the hospital after a fall. He had been diagnosed with CTX in his 30s and had had numerous complex-partial seizures, which occur in 50% of adult patients. Seizures were characterized by staring spells and speech deficits, occasionally generalizing to tonic-clonic leg movements. He had marked enlargement of the tongue and Achilles tendons (figure, A–D). Neurologic examination was notable for dementia, spasticity, and ataxia. Brain MRI revealed lesions in the temporal lobes, globus pallidus, and dentate nucleus of the cerebellum (figure, E, F), thought to be from lipid accumulation and reactive astrocytosis. Additionally, hemosiderin deposits with calcification were present in the cerebellar hemispheres (figure, G, H). Biochemical testing revealed a high plasma cholesterol level (3.04 mg/dL, >10 times normal). The patient had been treated with chenodeoxycholic acid, but did not receive it for over a year because of short supply worldwide. Lack of recent therapy was associated with an increased frequency of seizures, prominent tongue protrusion, and further enlargement of the Achilles tendons.

REFERENCES


Teaching NeuroImage: Nocardial intramedullary spinal cord abscess

A 79-year-old man with ulcerative colitis on chronic prednisone therapy developed severe midcervical pain and progressive weakness of the left arm and leg over several days. This was associated with left forearm paresthesias and urinary hesitancy and incontinence. He had no cranial or bulbar symptoms. On general examination, he was afebrile but there was midcervical spine tenderness. Neurologic examination revealed normal mental status and cranial nerves; strength was 2/5 on the left, and 4/5 on the right; there was a sensory level to pain and temperature on the right to C4, with reduced proprioception in the left foot and hand; there was a left Babinski sign and a mute right plantar response. White blood cell count was 18.2 × 10^9/L. Blood cultures were negative. Chest CT demonstrated multiple lung nodules. Cervical spine MRI (figure 1) revealed an intramedullary ring-enhancing mass on the left at C3-4 associated with edema from C2 to C7. Open spinal cord biopsy revealed Nocardia farcinica abscess (figure 2). Lumbar puncture and bronchoscopy were not performed. The patient was treated with IV trimethoprim-sulfamethoxazole and dexamethasone. After 10 days, lower extremity strength improved bilaterally. Left arm strength and sensory deficits remained unchanged. He died 8 weeks later due to cardiac arrest. No autopsy was performed.

CNS nocardiosis is usually associated with systemic nocardial infection. Although brain abscess is the most common presentation of CNS nocardiosis, rare cases of intramedullary spinal cord abscess have been reported.1,2 Nocardia abscess should be considered in immunocompromised patients with spinal cord syndromes. Expeditious tissue diagnosis and antibiotic therapy are essential to improved outcomes.

REFERENCES
The trainee book review section assesses the usefulness of books developed for use neurology residents and fellows. Reviews will be written primarily by upper-level residents, fellows or program directors that have appropriate perspectives on the potential value of the book at various levels of training.
Book Review

PSYCHIATRY FOR NEUROLOGISTS
edited by Dilip V. Jeste and Joseph H. Friedman,
436 pp., Humana Press, 2005, $135

Despite the close anatomic and clinical relationship between the fields of neurology and psychiatry, many neurologists do not feel equipped to manage the psychiatric symptoms of their patients. In answer to this problem, Psychiatry for Neurologists, edited by Dilip V. Jeste and Joseph H. Friedman, is intended as a practical resource for neurologists into those areas of clinical psychiatry that impact the management of neurologic patients.

This book, authored by neurologists, psychiatrists, and clinicians trained in both disciplines, lives up to its goals. It is a well-balanced, interesting and, above all, practical text on those topics in clinical psychiatry about which most neurologists wish themselves better informed. In addition, this book goes beyond the purely clinical into historical, ethical, and even legal issues.

The first part of the text describes the codevelopment of neurology and psychiatry from their shared roots in 19th century Europe to their renewed collaboration in the present day, highlighting the personalities that shaped their paths along the way. The second part summarizes the psychiatric evaluation of a neurologic patient, with an emphasis on and examples of the most common psychiatric symptoms of neurologic diseases.

The subsequent two sections form the greater part of the text. The third part of the book, composed of seven chapters, is devoted to the major psychiatric disorders that a neurologist is most likely to encounter, including depression, anxiety disorders, schizophrenia, hysteria or somatoform disorders, catatonia, addictions, and personality disorders. Each chapter covers the epidemiology, diagnosis, differential diagnosis, biology, course, and treatment of each disorder. Some of the chapters include interesting historical information related to the disorders. There is an emphasis throughout on the neurologic symptoms, the neurologic diseases that may mimic each disorder, and, when relevant, the neurologic side effects of treatment.

The fourth part of the book describes the common psychiatric symptoms and complications found in many neurologic diseases. The chapters include dementia, stroke, neuromuscular disorders, Parkinson disease, multiple sclerosis, epilepsy, Tourette syndrome, Huntington disease, and the often neglected psychiatry of the cerebellum. Each chapter is broken down into epidemiology, signs and symptoms, pathophysiology, differential diagnosis, course, and treatments. Several of the chapters have helpful cases and vignettes and most have tables and figures detailing psychiatric diagnostic testing and classification systems.

The final part of the book, called simply Other Topics, provides excellent and informative overviews of those grayest areas between neurology and psychiatry. Those topics include childhood disorders, geriatric disorders, fatigue, and an especially concise and useful chapter on delirium. The remaining chapters cover an assortment of topics helpful for practicing neurologists and include psychopharmacology, electroconvulsive therapy, neurosurgical treatment of psychiatric disorders, psychotherapy, management of psychiatric emergencies, and informed consent and competency. The last chapter outlines the case by case legal history of self-determination, informed consent, and refusal of treatment and explains competence and the laws of civil commitment.

Psychiatry for Neurologists is a well-written, practical, and comprehensive resource for anyone involved in the care of neurologic patients.

Reviewed by Megan Alcauskas, MD
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