MAYO CLINIC

NeurosciencesUpdate

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INSIDE THIS ISSUE

Multiple Sclerosis Mimickers: Recognizing the Underrecognized

For more than 100 years, neuromyelitis optica (NMO), known as Devic disease, was thought to be a variant of multiple sclerosis (MS), despite observations that acute episodes were restricted to the optic nerve and spinal cord and were more immediately devastating than in MS. It was not until 1999—when neurologists and MS specialists Brian G. Weinshenker, MD, at Mayo Clinic in Rochester, Minnesota, and Dean M. Wingerchuk, MD, at Mayo Clinic in Arizona, published a series of 73 cases and identified distinguishing features of NMO—that the disease began to be recognized as an entity distinct from MS.

NMO is perhaps the best known of the MS mimickers, a group of neurologic conditions that may share characteristics of MS but are being identified as discrete diseases. Patients may have radiologic findings consistent with MS but have symptoms that are not. Another distinguishing feature of MS mimickers is that standard MS treatments often fail. Although most such disorders are uncommon, their identification is of obvious clinical utility, and understanding them provides insights into CNS disease mechanisms shared across disease types.

Examples of MS Mimickers

Chronic Lymphocytic Inflammation With Pontine Perivascular Enhancement Responsive to Steroids

Early in his career, B. Mark Keegan, MD, a neurologist at Mayo Clinic in Rochester, saw a patient with signs typical of inflammatory brainstem disease, in whom MS was suspected. The MRI findings, however, showed small focal, gadolinium-enhancing lesions possibly more typical of CNS sarcoidosis but certainly highly atypical of MS (Figure). The condition was responsive to corticosteroids, but, unlike MS, the lesions recurred immediately after the patient was weaned from corticosteroid therapy.

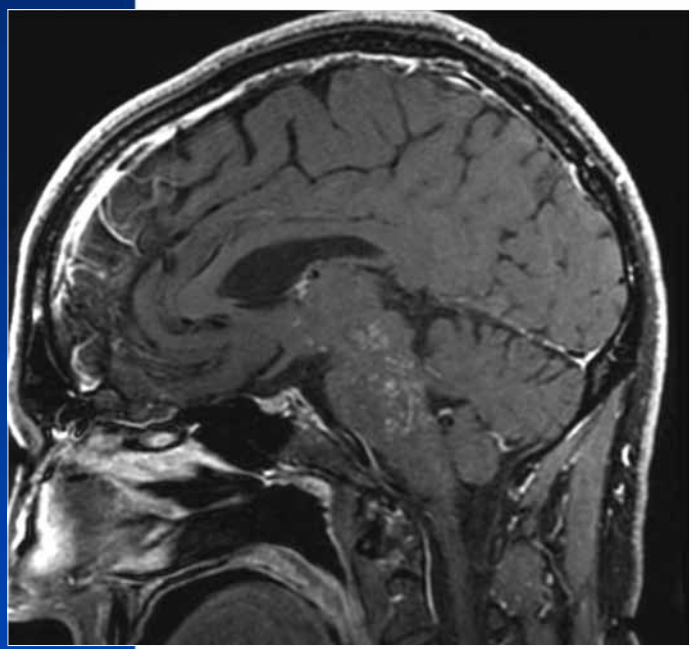

Figure. *Sagittal T1-weighted MR image with gadolinium showing multiple punctate perivascular enhancing lesions within the pons and midbrain, consistent with chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS).*


Brian G. Weinshenker, MD


Dean M. Wingerchuk, MD


B. Mark Keegan, MD


Sean J. Pittock, MD

"We ran multiple tests, but all of them came back negative for known entities. Fortunately, the neurosurgeon was able to conduct a biopsy of the brainstem, which showed a nonspecific inflammation," Dr Keegan explains. Ten years later, a neuroimmunology colleague, Sean J. Pittock, MD, brought a patient with similar signs to Dr Keegan's attention. Other patients with similar symptoms and the typical MRI findings soon followed, including two patients from Belgium. In four of the eight patients who underwent brainstem and cerebellum biopsy, the findings were similar and exclusive of other known diseases.

Drs Pittock and Keegan and their colleagues have since identified the common radiologic, pathologic, and clinical features of the disease they have labeled *chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids* (CLIPPERS) (Pittock et al. *Brain*. 2010;133[9];2626-34). The symptoms include episodic diplopia or facial paresthesias with subsequent brainstem and, occasionally, myelopathic symptoms that improve with a high dose of corticosteroids and may require long-term immunosuppressive therapy.

Primary Intramedullary Spinal Cord Lymphoma and Secondary Intramedullary Spinal Cord Non-Hodgkin Lymphoma

Myelopathies may complicate cancers such as lymphoma, but usually the clinical effect is due to an extramedullary compressive cause. Although rare, intramedullary spinal cord lymphoma can occur and mimic other intramedullary cord lesions, such as MS or NMO, even in the absence of systemic lymphoma, thus making the differential diagnosis difficult.

In a review of 14 such cases, Dr Keegan and his colleagues (Flanagan et al. *Neurology*. 2011;77[8]:784-91) found that patients presented with back pain (64%) and constitutional symptoms of fever, chills, malaise, night sweats, or weight loss (64%), and some had evidence of lower motor neuron involvement (43%). The diagnoses that were initially considered included MS, spinal cord neoplasia, infectious myelitis, NMO, transverse myelitis, sarcoidosis, acute disseminated encephalomyelitis, and chronic inflammatory demyelinating polyneuropathy. MRI findings showed multifocal, persistently (2-8 months) gadolinium-enhancing lesions with spinal cord enlargement, occasionally with extension into the conus medullaris and with accompanying brain lesions. Morbidity rate was high, and treatment was often delayed because the cause remained uncertain. In most patients, definitive diagnosis required brain or spinal cord biopsy.

Leptomeningeal metastases may complicate non-Hodgkin lymphoma (NHL), but intramedullary spinal cord metastases are rare. In a follow-up to the primary intramedullary spinal cord lymphoma (PISCL) study, Dr Keegan and colleagues (Flanagan et al. *J Neuro-Oncol.* Published online December 22, 2011) found direct intramedullary spinal cord infiltration in seven patients with active NHL. The investigators cautioned that when myelopathy is discovered in a patient with NHL, it is important to exclude other causes, such as myelopathy due to spinal cord compression or of paraneoplastic cause, infection, ischemia from intravascular lymphoma, and hematomyelia from damaged blood vessels and from the effects of irradiation on the spinal cord. Survival was poor in these patients (median survival, ~12 months), but even this survival was far better than in patients with spinal cord metastases from other solid cancers (median survival, ~3 months).

Paraneoplastic Isolated Myelopathy

Paraneoplastic myelopathies occur most commonly with cancer of the lung or breast. A Mayo Clinic retrospective review of 31 cases of paraneoplastic isolated myelopathy found that the disorder typically occurred in the context of other neurologic disorders, including encephalopathy, peripheral neuropathy, and cerebellar dysfunction (Flanagan et al. *Neurology*. 2011;76[24]:2089-95). An interesting spinal MRI finding that should alert physicians to the possibility of paraneoplastic myelopathy is symmetrical, longitudinally extensive tract or gray matter changes, called *tractopathies*.

Sporadic and Hereditary Leukoencephalopathy With Spheroids

Neuroaxonal leukodystrophy is a rare cause of progressive leukoencephalopathy, the primary symptom of which is dementia. The most frequently cited cases are those that are inherited and occur in childhood. When neuroaxonal leukodystrophy has an adult onset and occurs sporadically, the severe, progressive cognitive and motor impairments can be confused with other progressive dementias and primary movement disorders. It can also be confused with MS because of the presence of asymmetrical, diffuse, nonenhancing subcortical white matter lesions on MRI (Keegan et al. *Neurology*. 2008;70[13 Part 2]:1128-33).

Sporadic and hereditary diffuse leukoencephalopathy with spheroids (HDLS) is another CNS white matter disease that can present with dementia. Other signs include personality changes, depression, parkinsonism, and seizures. This autosomal dominant inherited disease mimics other neurodegenerative diseases,

including Parkinson disease (PD) and MS.

Elizabeth A. Shuster, MD, a neurologist and MS specialist at Mayo Clinic in Florida, saw a patient two years ago with signs of demyelinating disease whose mother had had a similar white matter disease. Because some of the clinical features were similar to PD, Dr Shuster consulted her neurology colleague Zbigniew K. Wszolek, MD, an expert in movement disorders who has a particular interest in neurodegenerative disease genetics. He had seen other patients with similar disorders. Working together with a team led by Mayo geneticist Rosa Rademakers, PhD, they were able to uncover the gene *CSF1R*, the loss of which appears to play an important role in HDLS (Rademakers et al. *Nature Genetics.* 2012;44[2]:200-5). *CSF1R* is considered a key mediator of microglial proliferation and differentiation in the brain, which suggests that microglial dysfunction is a critical mechanism in HDLS pathology.

As Dr Shuster points out, identifying MS mimickers helps to clarify disease commonalities. MS and many other neurologic conditions have both degenerative and inflammatory features. She notes that interest is growing, including among Mayo Clinic researchers, about the neurodegenerative aspects of MS and whether or not it shares common features with other neurologic disorders. As a step in this research process, she and Dr Wszolek are looking for links between the neurodegenerative aspects of PD and those of MS.

Neuromyelitits Optica Update

After the seminal paper on NMO in 1999, a Mayo team of neurologists and autoimmunity researchers had, by 2006, identified the NMO antibody (NMO–immunoglobulin [Ig] G) and its target, aquaporin-4, and had developed a diagnostic blood test that reliably distinguished NMO from MS. Now, NMO is recognized around the world as a distinct disease.

Dr Wingerchuk notes that the laboratory test for NMO-IgG helped to galvanize the MS community to recognize NMO as a unique disease and that it is not uncommon now for Mayo to receive referrals specifically for NMO evaluation. Treatment strategies for NMO differ from those used for MS, and Mayo Clinic investigators are studying the benefits of various new approaches for NMO. For patients with a severe relapse that is unresponsive to corticosteroids, plasma exchange is widely used as a rescue therapy. To investigate the value of plasma exchange as a preventive NMO therapy, Drs Wingerchuk and Keegan have established a prospective registry of patients who are being treated with maintenance plasma exchange as part of their routine care. The observational study will help determine how quickly and completely the antibody is depleted, how well that depletion is maintained, and whether maintenance plasma exchange successfully prevents relapses and disability.

In addition, Drs Pittock and Wingerchuk are heading up a clinical trial of eculizumab for NMO treatment. Eculizumab is a monoclonal antibody that targets complement, an immune system component thought to be a key early activator of inflammation in NMO relapses. Study results are expected later this year.

Finally, Drs Weinshenker and Wingerchuk are leading an international panel to revise and refine the diagnostic criteria for NMO. Mayo Clinic in Arizona is also participating with two other medical centers in developing a clinical consortium to facilitate multicenter collaboration for NMO research.

Elizabeth A. Shuster, MD

Zbigniew K. Wszolek, MD

Predicting Outcomes in Normal Pressure Hydrocephalus

Typically affecting elderly persons, normal pressure hydrocephalus (NPH) is one of the more difficult conditions to diagnose. In addition to gait difficulty and incontinence, the symptoms include cognitive impairment, which is often characterized as memory loss.

The cause of enlarged ventricles, found on CT or MR scanning, is uncertain. However, it has been shown experimentally to be associated with decreased absorption of spinal fluid, increased pulse pressure or systolic blood pressure (BP), or both, and brain atrophy. Neill R. Graff-Radford, MD, a neurologist at Mayo Clinic in Florida, and his neurosurgical colleague Robert E. Wharen Jr, MD, have a long experience in treating NPH and assessing factors that may predict outcomes.

Diagnosis and Treatment

After other causes of gait disturbance have been ruled out, patients at Mayo have a test that mimics a temporary shunt to determine whether decreasing cerebrospinal fluid volume improves

Neill R. Graff-Radford, MD

gait. Typically, 30 cc of fluid is removed during a spinal tap, and pre- and postprocedure videos of the patient walking are compared. Separately, tests for cognitive function are conducted to help determine if memory problems are isolated or are accompanied by other impairments. The presence of aphasia, for example, suggests an additional degenerative pathology that likely will not improve with shunting.

Treatment consists of a neurosurgically placed shunt that drains cerebrospinal fluid into the peritoneal cavity. Dr Wharen explains that one of the known complications in the past has been overdrainage, which can cause the brain to shrink and may result in subdural hemorrhage or subdural hygroma. The recent introduction of programmable shunt valves, however, has improved outcomes and reduced the need for additional surgical procedures to adjust the rate of drainage (Figure). Dr Wharen notes that NPH may have a degenerative component. Even in patients with initial success, it may be necessary to adjust the rate of drainage six months to several years later. The programmable valve readily enables such adjustments and has made surgery more viable for more patients.

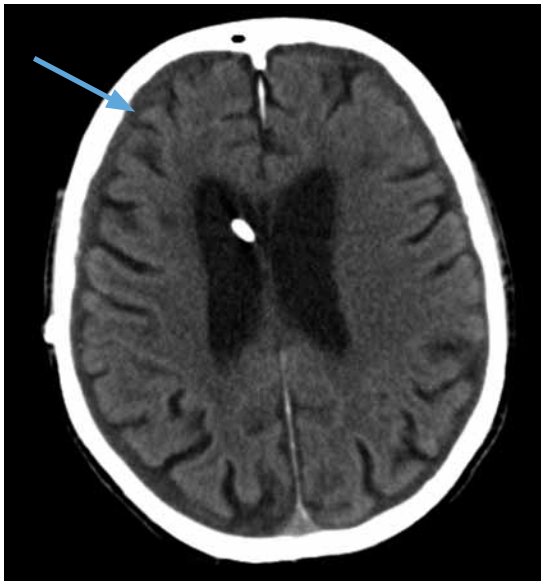

Figure. *CT scan of a patient with a subdural hygroma (arrow) and a shunt in place, illustrating overdrainage.*

Predicting Cognitive Outcomes

Not all symptoms improve with treatment. Often, gait and incontinence improve, but memory and cognition may not. Dr Graff-Radford has long suspected that overlapping conditions may be important to the cognitive decline associated with NPH. The presence of aphasia or even mild naming deficits may signal coexisting pathology, such as vascular disease or Alzheimer's disease (AD). As he points out, studies have shown that among people older than 74 years, the brain of more than 30% of patients shows evidence of AD pathology on autopsy. Cerebrovascular disease is also frequent in this age-group because hypertension is common. Several studies show that hypertension is associated with hydrocephalus in animal models and with hydrocephalus in humans.

Dr Graff-Radford and colleagues presented findings at the American Academy of Neurology meeting in New Orleans, Louisiana, in April, from data collected by the Atherosclerosis Risk in Communities (ARIC) Study, a prospective epidemiologic study sponsored by the National Heart, Lung, and Blood Institute. Looking at the MRI scans of study participants taken 10 years apart, he and his coauthors found that both increased systolic BP and increased pulse pressure correlated with increased ventricle size. In earlier research, Dr Graff-Radford and colleagues showed that head size also correlates with increased risk of NPH. Approximately 10% to 20% of people with NPH have a head size at or above the 98th percentile. Thus, it may be that people born with a large head have congenital hydrocephalus that becomes symptomatic as they age.

The question of the contribution of head size, vascular disease, and underlying AD pathologic factors is important to predicting outcomes for surgical shunting. To address these issues, Drs Graff-Radford and Wharen are initiating a prospective study in which 25 NPH patients who have agreed to shunt surgery will be given a battery of neuropsychological tests and PET imaging to screen for amyloid plaque build-up before surgery. They will also have gait evaluation and neuropsychological testing at one year follow-up. The goal of the study is to determine whether the presence of amyloid in the brain influences cognitive outcomes from shunt surgery in NPH. The investigators hope their findings will help physicians in counseling patients about which symptoms may improve with a shunt and whether shunting is a good option.

Pediatric Epilepsy at Mayo Clinic: Managing Seizures and Related Comorbidities

More than 300,000 US children younger than 15 years have epilepsy. More than 90,000 of them have intractable seizures. For children with epilepsy, seizures are often only one of the concerns. One in four children with epilepsy has some degree of intellectual disability. For children with intractable seizures, the frequency rises to one in two and the impairments tend to be more severe. Elaine C. Wirrell, MD, a pediatric neurologist specializing in epilepsy at Mayo Clinic in Rochester, Minnesota, notes that children with epilepsy are also at increased risk for mood disorders, depression, and anxiety."The best way to manage the risk of associated comorbidities is to treat the seizures themselves," she says,"but it is important to address seizures within the context of potential emotional and intellectual deficits."

Katherine C. Nickels, MD, Lori M. Cain, RN, Nicholas M. Wetjen, MD, Elaine C. Wirrell, MD, Lily C. Wong-Kisiel, MD, and Michael J. Zaccariello, PhD, LP

Nicholas M. Wetjen, MD, a Mayo pediatric neurosurgeon, agrees."Our goal is always to treat the epilepsy, but the surgical service here is very attentive to quality of life."When the seizure focus is in eloquent cortex, Dr Wetjen does his best to help parents weigh the benefit of seizure reduction against surgically induced deficits. He is aided in that effort by the pediatric neurology epilepsy specialists on the team, which, in addition to Dr Wirrell, includes Katherine C. Nickels, MD, Lily C. Wong-Kisiel, MD, and Lori M. Cain, RN.

Beyond Seizures: Comorbidities Associated With Epilepsy

Children with controlled seizures may appear normal, but they still have cognitive issues. For example, simply living with a chronic disease can generate anxiety, interfere with attention, and create social problems. In a review article, Dr Wirrell and coauthor L. D. Hamiwka, MD, of Ohio State University College of Medicine, state that comorbidities associated with pediatric epilepsy can impact not only the child, but also families (*J Child Neurol*. 2009;24[6]:734-42). Impairments in social, emotional, or intellectual processing and development have been found to vary with age of seizure onset, intractability, and anatomical locus of seizure focus. The earlier the age of onset, the greater the risk to the developing brain.

Edyth Strand, PhD, chair of the Division of Speech Language Pathology at Mayo Clinic, notes that seizures may affect areas of the brain important to language development and that language dysfunction can impede learning and inhibit social interaction during development. For example, Landau-Kleffner syndrome is a well-recognized disorder characterized by a sudden or gradual regression of language processing in conjunction with the onset of clinical or electrographic seizures. Sometimes, the first indication of a receptive language problem is difficulty recognizing familiar noises. Expressive speech and language can also be markedly impaired, especially when the syndrome appears during critical periods of speech acquisition.

Michael J. Zaccariello, PhD, LP, one of the neuropsychologists on the Mayo team, explains that neuropsychological assessment provides a snapshot of where on a scale of normal behavior a child is functioning relative to cognitive, behavioral, and emotional processing within the context of a complex neurologic condition. As he puts it,"We integrate the medical, cognitive, and psychosocial data for the family. Our goal is to help families, teachers, students, school administrators, and paraprofessionals understand how the child's epilepsy is impacting performance. We provide systematic recommendations on how to address weaknesses and maximize strengths."

Dr Nickels adds that armed with the results of cognitive testing, families feel"not only informed, but empowered."She notes that when a child's seizures are controlled by medication, families can mistakenly blame continued disabilities on antiepileptic medications. Although seizure frequency and

severity play a role in the duration of behavioral and intellectual deficits, it is the underlying neuropathology, not the seizures themselves, that affect development. Among the biologic factors that can impact emotional and cognitive function are structural brain abnormalities, irregularities in neurotransmitter pathways, and general or localized brain atrophy.

Interventions for Intractable Seizures Surgery

At Mayo Clinic, the surgical work-up can be done in one to two weeks. It includes state-of-the-art functional brain mapping and studies to determine the locus, frequency, severity, and duration of seizures and whether other medical conditions coexist with the seizures.

In-Patient Pediatric EEG Monitoring

Pediatric surgical candidates undergo EEG monitoring in Mayo Eugenio Litta Children's Hospital, the 85-bed pediatric facility located within Mayo's St. Marys Hospital in Rochester. Five pediatric rooms, as well as the pediatric intensive care unit, are hardwired with ceiling cameras for behavioral observation and continuous EEG monitoring via external or intracranial EEG leads. In-patient EEG video monitoring helps minimize risks associated with medication withdrawal, a process that is often required to record seizures. Monitoring may take from 24 hours to several days. Dr Wirrell also notes that unlike many centers, "Mayo not only records the EEG, but also has technicians monitoring the patient every second of the day or night. So, if the patient or family member is sleeping or the seizure is subtle, our technologists are still able to pick it up." Continuous, 24/7 monitoring by trained, on-site technicians increases safety and can reduce the length of stay on the unit.

The EEG video monitoring unit is designed so that an adult family member can stay with the child at all times. Although children are restricted to their room, they are free to move about within the room. The unit's rooms are equipped with the latest technology, including interactive computer games. Child-life specialists visit several times a day with crafts, toys, games, and videos and also work with children and families to help them through procedures that may be uncomfortable or are unfamiliar.

Localizing Seizure Focus Through SISCOM

SISCOM stands for subtraction ictal single-photon emission computed tomography (SPECT) coregistered to MRI. Pioneered by Mayo, it fuses the MRI image with the SPECT image, an innovation particularly useful in seizure localization. Dr Wong-Kisiel has a particular interest in the application of SISCOM to children with multifocal or indeterminate focal MRI or EEG findings. A SISCOM study involves a radioactive tracer that is injected by technologists as soon as possible during a seizure. Unlike adults, children are often unable to verbalize when they are having a seizure, so continuous EEG monitoring and observation are critical.

Ketogenic Diet

The ketogenic diet—a high-fat, low-carbohydrate diet that mimics the fasting state and stimulates the ketogenic metabolism pathway—was first used in the 1920s at Mayo Clinic. It has since been discovered to improve seizure control in children with intractable epilepsy, and more than 100 Mayo Clinic pediatric epilepsy patients are currently on the diet. Children who are candidates for the diet begin it during a three- or four-day stay in Mayo's pediatric hospital so their parents can learn to manage the diet and a child's response can be monitored before the child is discharged. Dr Nickels explains that although the diet is rigorous, families seem to adapt quickly. Mayo dieticians have designed more than 100 menus for families to download and are willing to create specific recipes on request.

Having the Time It Takes

Epilepsy is a group of disorders, and differential diagnosis requires, first and foremost, a lengthy, detailed history and clinical assessment. At Mayo, the evaluation may extend to include metabolic tests and evaluations by autoimmune neurology, genetics, and other subspecialty services. As Dr Zaccariello states, the clinical evaluation is comprehensive, and families can feel overwhelmed. He feels fortunate that Mayo allows him as much time as necessary to explain, interpret, and guide patients through the process. Those feelings are echoed by his fellow team members, who point out that there is always enough time for data from all subspecialties to be reviewed at the epilepsy team conference, to arrive at an agreed-upon treatment strategy. At Mayo, treatment of pediatric epilepsy means finding the best method of seizure control, as well as addressing related cognitive and psychosocial impairments.

Research Highlights in Neurology and Neurologic Surgery

Neurosciences Research

Probable REM Sleep Behavior Disorder Doubles Risk of Mild Cognitive Impairment and Parkinson Disease

A Mayo Clinic study has found that rapid eye movement sleep behavior disorder (RBD), in which people act out their dreams, may be an important risk factor for neurodegenerative disease. RBD has been associated with mild cognitive impairment (MCI) and synuclein disorders such as Parkinson disease (PD) and dementia with Lewy bodies. Previous Mayo Clinic studies estimated the five-year risk of developing a neurodegenerative syndrome to be 45%. These calculations were based on a clinical population referred to the sleep or movement disorders clinic. To determine the risk in the general population, Mayo Clinic researchers conducted a prospective study of cognitively normal patients aged 70 to 89 years, 44 of whom had probable RBD (pRBD) and 607 of whom did not. The patients were monitored for a median of 46 months. The research team found that pRBD confers a 2.2-fold increased risk of having MCI or PD within 4 years. The importance of the study is the identification of RBD as a risk factor for clinical and research purposes, particularly in developing future experimental trials for α-synuclein disease-modifying therapies and early intervention. The study was published in the *Annals of Neurology* (2012;71[1]:49-56). Authors: B. P. Boot, B. F. Boeve, R. O. Roberts, T. J. Ferman, Y. E. Geda, V. S. Pankratz, R. J. Ivnik, G. E. Smith, E. McDade, T. J. H. Christianson, D. S. Knopman, E. G. Tangalos, M. H. Silber, and R. C. Petersen.

Immunotherapy Associated With Improved Seizure Outcomes Among Patients with Autoimmune Epilepsy

Seizures can be a common symptom among autoimmune neurologic disorders, such as limbic encephalitis and multifocal paraneoplastic disorders. A retrospective study of 32 patients with a diagnosis of autoimmune epilepsy in the Mayo Clinic Autoimmune Neurology Clinic and at Mayo's Epilepsy Clinic found that 81% of patients continued to have daily seizures despite treatment with two or more antiepileptic drugs (AEDs). Twenty-seven patients were given immunotherapy, and after a median of 17 months of treatment, 22 (81%) of them reported marked seizure reduction. Of those, 18 patients (44%) were seizure-free within 12 weeks of immunotherapy. Five patients did not respond to immunotherapy. The authors concluded that early-initiated immunotherapy may improve seizure outcome when clinical and serological signs suggest an autoimmune basis for medically intractable seizures. They emphasize that in such cases, immunotherapy should not be used alone but in conjunction with AEDs to optimize seizure control. In an accompanying editorial, Gregory K. Bergey, MD, of Johns Hopkins University School of Medicine, noted that the true scope of autoimmune epilepsy in patients with drug-resistant epilepsy may not be known "but certainly at present is probably being underdiagnosed." He added that the Mayo study "is another reminder that we need to broaden our concept of symptomatic chronic epilepsy from the structural realm into more dynamic processes not limited to acute inflammatory or infectious pathologies (eg, meningitis or encephalitis)." The Mayo Clinic study was published in *Online First* by *Archives of Neurology* (Mar 26, 2012; doi:10.1001/archneurol.2011.2985). Authors: A. M. L. Quek, J. W. Britton, A. McKeon, E. So, V. A. Lennon, C. Shin, C. J. Klein, R. E. Watson Jr., A. L. Kotsenas, T. D. Lagerlund, G. D. Cascino, G. A. Worrel, E. C. Wirrel, K. C. Nickels, A. J. Aksamit, K. H. Noe, and S. J. Pittock.

Prospective Hemorrhage Risk in Patients With Intracerebral Cavernous Malformations

With the exception of prior hemorrhage, risk factors for prospective hemorrhage in patients with intracerebral cavernous malformations (ICMs) vary across studies, and debate continues about the influence of sex, ICM locus, and number of ICMs. To address these conflicting results, Mayo Clinic researchers conducted a study aimed at determining prospective hemorrhage risk in a large population of patients who had long-term follow-up. The retrospective study included 292 patients who had a diagnosis of ICM as identified by MRI. Of the study patients, 62% presented with symptoms related to ICM and 5% had symptoms that were of unclear relationship to the identified ICM. In 33% of patients, the discovery of the ICM was incidental. When patients were grouped by initial presenting symptom, results revealed that the annual risk of hemorrhage is low when the ICM was an incidental finding and that in patients with prior hemorrhage, the risk is initially high but decreases over time. Prior hemorrhage and multiple ICMs were found to be significant risk factors for future hemorrhage, as noted in previous studies. In contrast to previous studies, pregnancy did not appear to be a risk factor and male sex did. The authors suggest that a biologic reason for this latter finding is not clear and that it may have been due to chance. The results may help in counseling patients with ICMs about the risks and benefits of ICM intervention. The study was published in *Neurology* (2012;78[9]:632-6). Authors: K. D. Flemming, M. J. Link, M. J. H. Christianson, and R. D. Brown.

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Clinical Trials Update

Study of Thymectomy in Acetylcholine Receptor-Positive Myasthenia Gravis: Patients with generalized MG with or without treatment with Mestinon and Prednisone are randomly assigned to receive thymectomy or not and are observed for three years.

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Inpatient Video-EEG Monitoring for Epilepsy
Continuous video-EEG monitoring (inpatient) helps localize seizure focus, determine seizure type, and quantify the number of seizures in patients with intractable recurrent seizures and those with an unconfirmed seizure diagnosis.
Optimizing the Functional Performance of Cancer Survivors
There is a growing understanding of the importance of exercise and rehabilitation for cancer survivors. Physical Medicine specialists can help patients manage the negative long-term sequelae of cancer and its treatments and obtain a more satisfying, high-quality recovery.
New Endoscopic Treatment for Severe Gastrointestinal Bleeding
Endoscopic ultrasound-guided therapy appears to be a safe and effective treatment for patients with severe gastrointestinal bleeding for whom conventional therapies have failed. The therapy involves injecting various agents directly into the source to stop the bleeding.
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A Mayo Clinic study suggests that removing the entire kidney from younger patients

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