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## Patient Selection: A Key Factor in Surgery for Degenerative Spinal Deformity

“While some of my most satisfied patients are adults who have had surgical correction for thoracolumbar spinal deformities, careful patient selection is critical to successful outcome,” explains Mark A. Pichelmann, MD, a neurosurgeon at Mayo Clinic in Rochester, Minnesota.

The past decade has seen advances in surgical techniques and instrumentation for the correction of adult spinal deformity, but it remains a complex and lengthy procedure. The risks associated with it are relatively high, so age, medical comorbidities, the nature and severity of the deformity, and the level of support during the lengthy recovery period must be carefully considered and evaluated. At Mayo, candidacy for the surgery typically includes evaluation by specialists in internal medicine and in physical medicine and rehabilitation (PM&R), as well as neurology and neurosurgery.

### Disease Classification

Many people have some degree of curvature of the spine, or scoliosis, yet are asymptomatic. Symptoms include back pain, physical deformity, and nerve compression, which can generate numbness, weakness, and leg pain, especially upon standing or walking. In some cases, and particularly as people age, the symptoms can be severe enough that they seek surgery.

Curvature of the spine in adults has been classified into two main types. Progressive scoliosis in people who had adolescent idiopathic scoliosis (AIS) that was either asymptomatic or minimally symptomatic until later in life is called *Type I adult scoliosis*. Symptoms may develop in response to accelerated curve progression due to subsequent degenerative changes or as a result of previous spine surgeries. Persons with the second type of scoliosis, called *Type II adult scoliosis*, have curvature of the



**Figure 1.** Preoperative adult degenerative scoliosis with curve progression and neurologic symptoms.



Mark A. Pichelmann, MD

spine as adults, most commonly in response to degenerative disease of the spinal column or, less frequently, in response to abnormalities that are not spine specific, such as osteoporosis, leg length discrepancy, or previous spine surgeries. Osteoporosis, for example, may weaken the bones of the spine enough to create small fractures that can result in asymmetrical spinal strength and cause the spine to bend toward the weaker side.

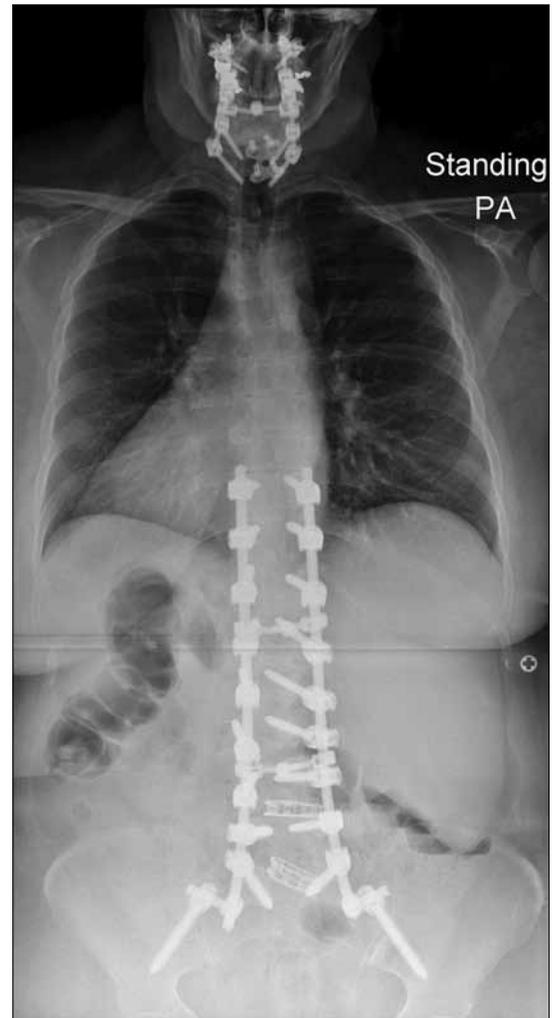
In a majority of patients with AIS, some progression of spinal curvature develops after they reach 40 years of age. The curvature progression in Type II adult scoliosis with degenerative characteristics can occur at a much more rapid pace than in Type I adult scoliosis.

### Surgical Candidate Evaluation at Mayo Clinic

The degree of curvature is just one factor in the decision to proceed to surgery. Other factors include the risk of curvature progression, physical and cosmetic effects of the deformity, and spinal balance. For example, healthy adults with curvatures of greater than 50° who are younger than 40 years of age may have relatively mild symptoms but may be good surgical candidates because of the propensity for the curvature to progress. Older patients more often seek surgical advice as a result of neurologic symptoms (eg, leg pain or weakness) than for the deformity itself.

Preexisting conditions such as diabetes mellitus, heart disease, osteoporosis, a history of smoking, and respiratory conditions are comorbidities that can increase the risk of postsurgical complications. Age is another major factor. “I usually tell my patients who are in their late 60s that risks are higher of having a minor or major complication as a result of having surgery. In some groups, there is approximately a 70% chance of a minor complication, such as a urinary tract infection or minor case of pneumonia, following surgery, but there is also an approximately 20% to 30% chance that they will have a major complication, such as wound infection, instrumentation failure or fracture, or some other medical complication, that prolongs their recovery.”

Surgical correction involves fusion to prevent progression and to alleviate nerve compression (Figures 1 and 2). Fusion may include an area from the low thoracic spine to the sacrum or, in some cases, a portion of the lumbar spine. For this reason, Dr Pichelmann often has his



**Figure 2.** Postoperative thoracolumbar fusion with curve correction and resolution of neurologic symptoms.

patients seen by occupational and physical therapy in PM&R before surgery so that the patients can understand the physical limitations surgery will impose. He believes that patients receive great benefit from being thoroughly informed about the ways in which a rigid spine will affect common activities of daily living. Dr Pichelmann finds it is also critical to ask patients about their support at home for the recovery period, which can last from many months to even a year or more after surgery.

In carefully selected patients, surgery can be a satisfying and effective management strategy. At Mayo, if surgery is not a viable option, patients receive a multidisciplinary treatment approach to their symptomatic scoliosis that may include specialists in anesthesiology, psychology, and the Pain Rehabilitation Center.

## Concussion: Determining When the Brain Has Recovered

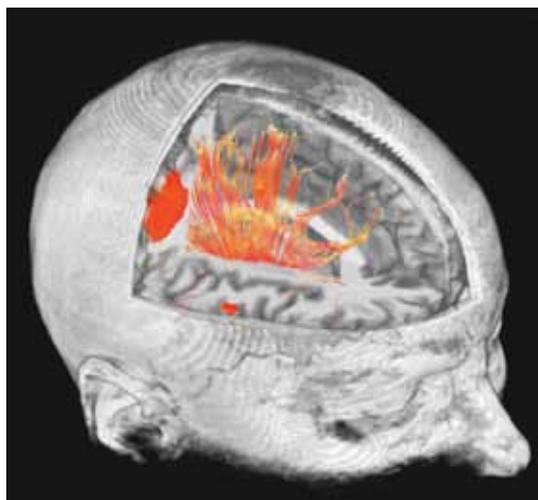
A sudden stop, a blow to the body, or a sharp twist of the head may make an athlete feel momentarily dazed, dizzy, or nauseated. Typically, the athlete would play through these symptoms or return to play as soon as he or she felt better. Yet, days and months later, that same athlete could be plagued by headaches, difficulty concentrating, and mood swings.

Mental exertion or a return too early to physical activity before a brain injury is resolved can worsen symptoms and puts athletes at increased risk for repeat injury with potentially permanent neurologic consequences. Until fully recovered, the brain is in crisis. Injured again, the crisis could turn life threatening. Second-impact syndrome, a rare but usually fatal syndrome predominantly affecting young male athletes under the age of 18 years, is a devastating consequence of returning athletes to play before complete recovery.

Determining when the brain has fully recovered is critical to the long-term health and even survival of someone who has sustained an initial concussion. The Department of Neurology at Mayo Clinic in Arizona is addressing this and other issues surrounding concussion by offering complimentary baseline and after-injury computerized cognitive testing to all athletes of high school and middle school age in the state. In addition, the department has founded a new Comprehensive Concussion Program and is working to develop a sports neurology subspecialty for neurologists nation-wide.

### Complimentary Baseline Cognitive Testing From Mayo Clinic

In the face of heightened public concern about concussion, several states have mandated through legislation that athletes recognized as experienc-



### Fact:

Most sports-related concussions are never diagnosed because athletes may not recognize or report the symptoms of concussion.

ing a concussion be immediately removed from play and not allowed to return to play until evaluated and cleared by a licensed health care provider. However, without an objective measure, such diagnostic decisions are difficult even for those providers with expertise in dealing with brain injury. Results of the neurologic examination may be normal. Standard imaging, such as CT and MRI of the brain, lacks the resolution to show microscopic structural and metabolic changes in the recovering brain. And the subjective assessment of athletes, many of whom do not recognize the connection between their symptoms and a concussion or fail to report their symptoms in the interest of returning to their sport, can be unreliable.

Cognitive testing is often the only viable and objective measure of impairment and recovery, but to be effective, it must be measured against an individual's preinjury baseline. Administered online, the cognitive baseline and after-injury test takes about 10 minutes to complete. It assesses skills such as memory, attention, learning, reaction time, and processing speed. Students can share the results with coaches, athletic trainers, and the health care provider of their choosing. In its first month of distribution, more than 25,000 athletes completed the testing.

"While advances in helmets and protective equipment are important, there is a limit in their capacity to prevent concussion, and we may be nearing that limit," says David W. Dodick, MD, a neurologist at Mayo Clinic in Arizona, director of the Comprehensive Concussion Program and president of the American Headache Society. "Educating athletes, coaches, parents, and athletic trainers about the symptoms, signs, and potential long-term effects of concussion and repeated concussion is critically important. Preventing concussion is as important



David W. Dodick, MD

as detecting it. Emphasizing the importance of mutual respect among players, eliminating head hits and fighting, and teaching young athletes involved in collision sports how to deliver and absorb a body check or tackle will go a long way to minimizing the frequency of concussion.” He also notes that it is important to be aware that children are particularly vulnerable to concussion. The developmental and maturational changes that occur in the brains of children appear to render them vulnerable to concussion, with symptoms that may take longer to resolve. In addition, concussions are more frequent in female athletes than male athletes, possibly because of their smaller neck girth, which does not provide the stability required to prevent the angular or rotational acceleration of the head that is a common mechanism of concussion.

As Dr Dodick puts it, “Injured brains need rest—both cognitive and physical.” He notes that recovery typically takes more time in a child than an adult. He goes on to say, “Not only is the developing brain more susceptible to injury, but an injury of similar magnitude will have a greater impact on a 12-year-old child than a 28-year-old adult. Repeated concussive injury can affect cognitive development, with consequences for learning and future employment. The concussed brain is a brain in crisis, and even a return to cognitive activities at school can stress the brain, amplify symptoms, and prolong recovery.”

## Fact:

Annually, 3.8 million children and adults in the United States experience a sports-related concussion.

### **Comprehensive Concussion Program at Mayo Clinic in Arizona**

As part of its commitment to patients with concussion, Mayo Clinic in Arizona has established the Comprehensive Concussion Program, led by Dr Dodick. Reflecting the three shields of Mayo Clinic, it focuses on patient care, education, and research. The care of patients treated through the program will be managed by an interdisciplinary team that includes 13 subspecialties.

This past August, in conjunction with Arizona State University and Phoenix Children’s Hospital, Mayo Clinic in Arizona held a concussion education and awareness summit designed to educate the general public, athletes, athletic trainers and directors, coaches, and health care providers about concussion. The day the concussion summit was held was proclaimed “Arizona Concussion Awareness Day” by the Governor of Arizona.

The Comprehensive Concussion Program will also conduct research. Working with clinical researchers at Mayo Clinic in Rochester, Minnesota, Dr Dodick and colleagues are beginning a prospective study in Junior A League hockey players to evaluate the correlation between clinical,

## Fact:

Among people who are 15 to 24 years old, sports are second only to motor vehicle crashes as the leading cause of traumatic brain injury.

imaging, and serum biomarkers and in-helmet g-force measurements and outcomes following concussion. Dr Dodick is also working with his colleagues in Arizona on developing research protocols to evaluate the cellular pathophysiology of concussion; identify clinical, imaging, or neurophysiological biomarkers that are diagnostic for concussion; and identify risk factors and prediction models for persons at risk for long-term neurologic sequelae (eg, dementia, stroke, psychiatric disease). In the future, for example, there may be an imaging signature on proton MR spectroscopy that indicates when an individual’s brain has actually recovered from concussion, rather than relying on subjective reporting of symptoms or on subtle or absent findings on the physical examination. Dr Dodick points out that evidence in the experimental and imaging literature shows that it takes much longer for the brain to recover from concussion than outward symptoms might suggest. “Right now, we’re dependent on measures that require us to infer recovery. I want to know not only when athletes tell me they’re back to baseline, but when their brain has returned to its metabolic baseline. It’s all about when the athlete’s brain is safe to return to play.”

### **Sports Neurology Subspecialty**

Dr Dodick and his colleagues are collaborating with four other institutions to become among the first programs to offer accredited fellowships in sports neurology. Currently, most sports medicine programs are part of a physical medicine and rehabilitation or orthopedic practice and focus on the physical aspects of recovery. A sports neurology program would bring neurologic expertise to the practice of managing athletic injuries related to concussive brain injury, among other neurologic aspects of athletic participation, such as peripheral nerve injury and neuromuscular and movement disorders.

## Meeting the Challenges of Myasthenia Gravis at Mayo Clinic in Florida

With the addition of Juan J. Figueroa, MD, there are now five neurologists specializing in neuromuscular disease at Mayo Clinic in Florida. “Each of us in the neuromuscular practice routinely treats patients with early diagnosis of myasthenia gravis, as well as those with more complicated symptoms that may be difficult to diagnose or may be refractory to standard treatments,” says Devon I. Rubin, MD.



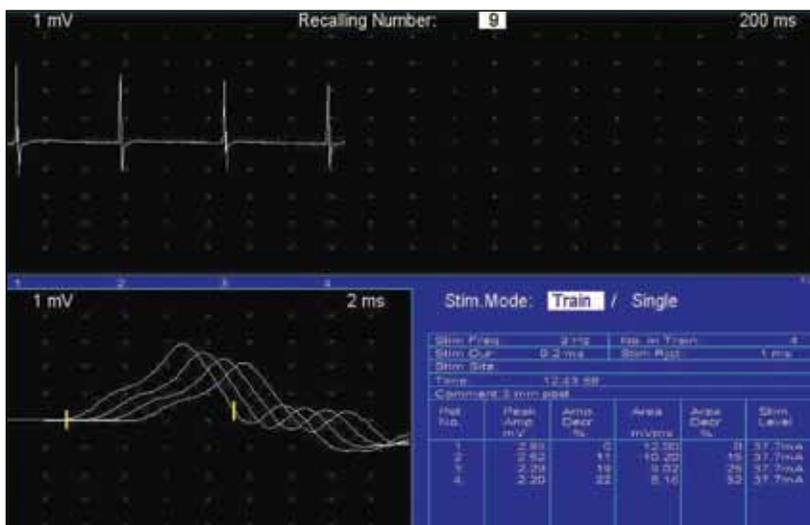
Devon I. Rubin, MD

The management of myasthenia gravis (MG) can be challenging. Response to treatment can vary widely within and across patients. While some patients have classic symptoms and respond well to first-line medications, others present with unusual distributions of weakness or test negative for the typical antibodies, which can complicate the diagnosis. Even for patients with a definitive diagnosis, MG may vary over time in its response to medication. Management requires careful monitoring of the potency, duration, and type of medication offered. Experienced neuromuscular clinicians can help determine the best combination of therapies for routine care and specialized treatments of symptom exacerbation and crisis management.

### Integrated Diagnosis

Mayo Clinic pioneered discoveries in the mechanisms of MG, distinguishing it from other, related neurologic autoimmune disorders, and developed many of the clinical tools to manage it. Across Mayo, diagnosis integrates the expertise of neurologists to conduct the physical examination and EMG testing, neuro-ophthalmologists to distinguish ocular muscle symptoms of MG from other ocular muscle conditions, immunologists to detect the serum antibodies associated with MG, radiologists to interpret imaging studies of the thymus, and thoracic surgeons to help determine whether thymectomy is a necessary or viable treatment option.

Neuromuscular neurologists at Mayo conduct repetitive stimulation studies, as well as single-fiber EMG, considered the most sensitive electrodiagnostic test of neuromuscular transmission (Figure 1). Both tests require specialized skill not only to administer, but also to interpret.



**Figure 1.** Abnormal decrement with repetitive stimulation nerve conduction studies in a patient with generalized myasthenia gravis.

“Single-fiber studies are very helpful in diagnosing mild disease when other tests fail to demonstrate abnormalities,” explains Dr Rubin. “For example, if someone has a slight eyelid droop or a mild case of double vision, the single-fiber EMG is extremely valuable in helping to confirm the diagnosis of mild MG.”

His neurology colleague Elliot L. Dimberg, MD, adds, “Most patients with MG have ocular findings—ptosis or diplopia—regardless of whether or not they have weakness in the extremities or extensor muscles or difficulty in speech, swallowing, or respiration. We’re fortunate to have Dr Paul Brazis, our neuro-ophthalmologist, to differentiate ocular muscle symptoms suspicious for MG from other types of ocular conditions.”

Diagnosis includes testing for antibodies associated with MG, such as acetylcholine receptor antibodies (AChR), which block acetylcholine receptors at the postsynaptic neuromuscular junction (Figure 2). In patients who test seronegative for AChR, further antibody analysis may include a test for muscle-specific kinase (MuSK), a relatively new antibody associated with MG. Patients who test positive for MuSK respond less consistently to traditional therapies and often have more bulbar than extremity involvement in their symptom presentation.

In discussing the resources available for patients with uncertain diagnosis, Kathleen D. Kennelly, MD, PhD, cites Vanda D. Lennon, MD, PhD, director of the Neuroimmunology Laboratory at Mayo Clinic in Rochester, Minnesota.



Elliot L. Dimberg, MD



Kathleen D. Kennelly, MD, PhD



Vanda D. Lennon, MD, PhD

Dr Lennon and her colleagues developed many of the antibody tests for MG, some of which are available only through Mayo laboratories. Dr Kennelly says, “When we have patients with a questionable diagnosis who test negative for both MuSK and AChR, Dr Lennon is very aggressive in conducting testing for other antibodies that may be associated with different neurologic disorders that cause weakness, such as Lambert-Eaton syndrome, and in working with and going the extra measure for the clinician. It is truly individualized diagnostic testing. She has more than once made the difference for our patients.”

### Meeting Treatment Challenges

Patients with MG have variability in response to treatment. At Mayo Clinic, immunomodulatory medications are often prescribed to enhance immunosuppression against the antibodies causing the disease. For patients with complex disease—those who test seronegative or who have an unusual distribution of weakness—MG management can be a difficult balance. As Dr Kennelly puts it, “We are advocates for the patient. For those with severe disease, we try novel therapies and medication combinations.”

Depending on the health of the patient, severity of the disease, response to treatment, or if a thymic tumor is present, a thymectomy may be recommended. John A. O’Dell, MD, the thoracic surgeon who works with the neurology team in Florida, has years of experience in thymectomy for patients with MG.

### Streamlining Care

With the new hospital now open on Mayo’s campus in Florida, care of patients with diagnosed and undiagnosed MG has become streamlined.

Dr Dimberg notes that many patients with undiagnosed MG present to the hospital’s emergency room. With the EMG laboratory located in close proximity to the inpatient service, diagnosis can be rendered, emergent management offered, and follow-up care provided in a seamless process.

### Ambulatory Infusion Center

For patients in an acute MG crisis, intravenous immunoglobulin or plasma exchange may be prescribed. And, although rare, there are some patients who require ongoing treatments of this type. “It is critical that you have an experienced ambulatory infusion center where this type of treatment can be administered on an outpatient basis,” says Dr Rubin. Mayo’s infusion center in Florida is open on weekends, and both it and the plasma exchange unit are staffed by nurses and technicians who are experienced in treating patients with MG.

### Muscular Dystrophy Association Clinic

Mayo Clinic in Florida is a designated site of the Muscular Dystrophy Association (MDA). Although the common perception is that the MDA is focused only on hereditary muscular dystrophies, it also advocates for patients with acquired neuromuscular diseases, such as MG and polymyositis. The Florida team monitors a number of patients through the MDA-sponsored neuromuscular clinic who for insurance reasons might not otherwise be able to receive care through Mayo. As Dr Kennelly points out, “We often share patients with neurologists at a distance who send patients for additional treatment advice. MDA support can make it easier for some of those patients to be seen here.”

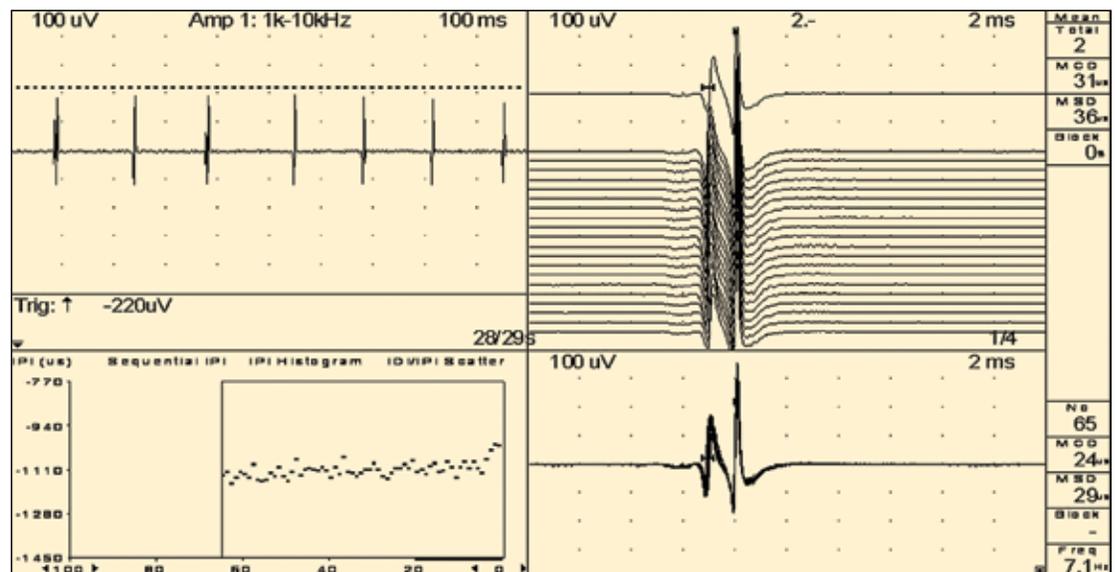


Figure 2. Normal jitter on a single-fiber EMG study.

# Research Highlights

## Genetic Mutation Linked to Parkinson's Disease

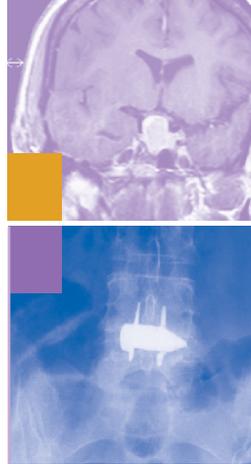
A team of Mayo Clinic neuroscientists, with collaborators from the United States, Canada, Europe, United Kingdom, Asia, and the Middle East, have identified mutations in VPS35, a protein responsible for recycling other proteins within cells. Mutations in VPS35 may impair the ability of a cell to recycle proteins as needed. This aberration could lead to the kind of errant protein buildup seen in Parkinson's disease and in other neurodegenerative diseases, such as Alzheimer's disease. Investigators used a new genetic sequencing technique called *exome sequencing* to look for shared variations in a pair of first cousins from a large Swiss family affected by Parkinson's disease. The study was published in the *American Journal of Human Genetics* (2011 Sep 9;89[3]:398-406). Authors: M. C. Chartier-Harlin, J. C. Daxsel, C. Vilariño-Güell, S. J. Lincoln, F. Leprêtre, M. M. Hulihan, J. Kachergus, A. J. Milnerwood, L. Tapia, M.-S. Song, L. E. Le Rhun, E. Mutez, L. Larvor, A. Duflot, C. Vanbesien-Mailliot, A. Kreisler, O. A. Ross, K. Nishioka, A. L. Soto-Ortolaza, S. A. Cobb, H. L. Melrose, B. Behrouz, B. H. Keeling, J. A. Bacon, E. Hentati, L. Williams, A. Yanagiya, N. Sonenberg, P. J. Lockhart, A. C. Zubair, R. J. Uitti, J. O. Aasly, A. Krygowska-Wajs, G. Opala, Z. K. Wszolek, R. Frigerio, D. M. Maraganore, D. Gosal, T. Lynch, M. Hutchinson, A. R. Bentivoglio, E. M. Valente, W. C. Nichols, N. Pankratz, T. Foroud, R. A. Gibson, F. Hentati, D. W. Dickson, A. Destée, and M. J. Farrer.

## Expansion of a Repeat in the Gene *C9ORF72* Linked to Pathogenesis of Frontotemporal Dementia and Amyotrophic Lateral Sclerosis

North American investigators led by neuroscientists at Mayo Clinic in Florida have found a genetic abnormality they say is the most common cause of two different, but related, familial forms of neurodegenerative disease. Several families have been reported with autosomal-dominant frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), genetically linked to chromosome 9p21. The study reports an expansion of a repeat in the gene *C9ORF72* that is strongly associated with disease in a large FTD/ALS kindred, previously reported to be conclusively linked to chromosome 9p. This same repeat expansion was identified in the majority of families with a combined FTD/ALS phenotype and TDP-43-based pathology. Analysis of an extended clinical series found the *C9ORF72* repeat expansion to be the most common genetic abnormality in both familial FTD (11.7%) and familial ALS (23.5%). The repeat expansion leads to the loss of one alternatively spliced *C9ORF72* transcript and to formation of nuclear RNA foci, suggesting multiple disease mechanisms. These findings indicate that repeat expansion in *C9ORF72* is a major cause of both FTD and ALS. This study was published online in the September 21 issue of *Neuron* (2011;72[2]:1-12). Authors: M. DeJesus-Hernandez, I. R. Mackenzie, B. F. Boeve, A. L. Boxer, M. Baker, N. J. Rutherford, A. M. Nicholson, N. A. Finch, H. Flynn, J. Adamson, N. Kouri, A. Wojtas, P. Sengdy, G. R. Hsiung, A. Karydas, W. W. Seeley, K. A. Josephs, G. Coppola, D. H. Geschwind, Z. K. Wszolek, H. Feldman, D. S. Knopman, R. C. Petersen, B. L. Miller, D. W. Dickson, K. B. Boylan, N. R. Graff-Radford, and R. Rademakers.

## SISCOM in Children With Tuberous Sclerosis Complex-Related Epilepsy

Mayo Clinic researchers assessed complete resection of a hyperperfusion abnormality found on subtraction ictal SPECT coregistered to MRI (SISCOM) correlated with seizure-free outcome in six children with tuberous sclerosis complex-related epilepsy. The median seizure onset age was 4 months (range, 1 day to 16 months). The age at the time of surgery ranged from 8 months to 13 years. A dominant SISCOM hyperperfusion focus was identified in five patients with multiple tubers. SISCOM provided additional localizing information for epilepsy surgery in three patients with nonlocalizing or discordant electrophysiologic and neuroimaging findings. At a minimum of 2 years' follow-up, three patients were free of seizures overall. Freedom from seizures was associated with complete resection of SISCOM-identified abnormality in two patients. These findings demonstrate that SISCOM can be useful in identifying the epileptogenic zone and in guiding the location and extent of epilepsy surgery in children with tuberous sclerosis complex and multifocal abnormalities. In children with tuberous sclerosis complex and intractable epilepsy, complete resection of the SISCOM-identified hyperperfusion abnormality is associated with freedom from seizures. This study was published in *Pediatric Neurology* (2011;45[2]:83-8). Authors: M. S. Aboian, L. C. Wong-Kiesel, M. Rank, N. M. Wetjen, E. C. Wirrell, and R. J. Witte.



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# Resources

[mayoclinic.org/medicalprofs](http://mayoclinic.org/medicalprofs)

Clinical trials

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## CME

Please join the Mayo Clinic Neurology and Neurosurgery Continuing Medical Education (CME) Facebook group. To join, search Facebook for Mayo Clinic Neurology and Neurosurgery Continuing Medical Education (CME). This group provides CME course information and updates, along with short video interviews with speakers and course directors.



## Clinical Trials Update

1. Study of Dichlorphenamide in Periodic Paralysis. Double-blind, placebo-controlled study of dichlorphenamide (Darandine) for treatment of hypo- or hyperkalemic periodic paralysis.
2. Study of Thymectomy in Acetylcholine Receptor-Positive Myasthenia Gravis. Patients with generalized myasthenia gravis with or without treatment with Mestinon and prednisone are randomly assigned to receive thymectomy or not and observed for three years.

For more information about other Mayo Clinic research studies, please visit: <http://clinicaltrials.mayo.edu/>.



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## Expedited Patient Referrals to Mayo Clinic Departments of Neurology and Neurologic Surgery

While Mayo Clinic welcomes appointment requests for all neurologic and neurosurgical conditions, patients with the following conditions are offered expedited appointments:

1. Cerebral aneurysms
2. Cerebral or spinal arteriovenous malformations
3. Brain, spinal cord, or peripheral nerve tumors
4. Epilepsy with indications for surgery
5. Carotid disease

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