Nationwide Expertise in Complex Spinal Surgery

Surgery to correct spinal deformity is inherently complex, posing risks to critical neurovascular structures and requiring experience in bone fusion and other orthopedic techniques. All three Mayo Clinic campuses have neurosurgeons with additional training in spinal deformity. As a major tertiary center, Mayo Clinic can provide enhanced expertise for adult and pediatric patients with severe spinal deformity.

“Our focus is not just a single specialty, but spine surgery itself,” says Jamal McClendon Jr., M.D., a consultant in Neurologic Surgery at Mayo Clinic in Phoenix/Scottsdale, Arizona. “Our additional training in spinal-deformity surgery gives us a greater appreciation for bone physiology and biology, and the desired outcomes for a bone fusion operation.”

“No matter where you are in the United States, Mayo Clinic has a specialist who focuses on spinal deformity,” adds Jeremy L. Fogelson, M.D., a consultant in Neurologic Surgery at Mayo Clinic in Rochester, Minnesota. “The operating room teams are dedicated to spinal surgery, so they’re very comfortable treating highly complicated spinal deformities.”

Wide range of conditions

At all three Mayo Clinic campuses, the spinal-deformity practice treats pediatric and adult patients with scoliosis, flat back syndrome, kyphosis and problems due to failed spinal fusions performed elsewhere. “We treat all spinal deformities, from the skull down to the sacrum,” Dr. Fogelson says.

Deformity-surgery training is especially beneficial in cases that require changing the alignment of the spine, such as an osteotomy in the cervical or lumbar spine (Figures 1 and 2). “A lot of patients with scoliosis have sagittal or coronal balance problems in addition to their scoliosis. Depending on how stiff the spine is, we might have to do an osteotomy — essentially, taking the patient’s spine apart in one place.

Figure 1. A. X-ray shows severe spinal deformity before surgical correction at Mayo Clinic. B. Post-surgery X-ray shows spinal alignment.
and then putting it back together in a configuration that better balances the spine,” says Mark A. Pichelmann, M.D., a consultant in Neurologic Surgery at Mayo Clinic in Jacksonville, Florida.

Working within a single institution, the spinal surgeons are able to consult with one another on particularly challenging cases. “Our neurosurgical training is crucial because we are working around nerves. But having the dual training with spinal-deformity surgery really helps us to do the optimal surgery for each patient,” Dr. Fogelson says.

In the past, children with spinal deformities generally have been treated at Mayo Clinic’s campus in Minnesota. However, neurosurgeons at Mayo Clinic’s campus in Florida treat patients age 16 and older, and Mayo Clinic’s campus in Arizona collaborates with Phoenix Children’s Hospital to provide spinal surgery for children pre- and post-puberty. “Our practice is growing, with patients of all ages,” Dr. McClendon says.

Specialized treatment teams
At Mayo Clinic, highly specialized treatment is provided before, during and after spinal surgery. “I often send my patients preoperatively to a physiatrist who is dedicated to spinal care. It’s helpful for patients to know what they can expect postoperatively in terms of functional limitations and how to work with those limitations,” Dr. Pichelmann says.

Patients are counseled before surgery on weight loss and smoking cessation, to lower the risk of surgical complications. Cardiologists or pulmonologists are consulted as necessary to assess patients’ readiness for surgery. “We also work with our endocrinologists to optimize patients’ bone marrow density and to ensure their bones are strong enough to tolerate surgery,” Dr. Fogelson says.

During surgery the treatment team includes neuroanesthesiologists, neuroradiologists and nurses with spinal-surgery expertise. “We have the full spectrum of safety precautions available — intraoperative monitoring, to make sure the patient doesn’t have new nerve or spinal cord damage; navigation systems to guide the placement of screws; and CT scans in the operating room to check our screw placement,” Dr. Fogelson says. “Sometimes we have two experienced surgeons working together to complete the procedure as quickly as possible, because we know that lengthy surgery can lead to complications.”

After surgery, patients are treated in neuro-intensive care units, and have inpatient physical therapy. Nurses work to have patients up and moving as soon as possible, and are experienced in preventing post-surgery pneumonia and thrombosis. An acute pain service is available to manage postoperative pain.

“Although these are highly complex cases, we’re very familiar with treating them, at all of our campuses,” Dr. McClendon says. “I don’t know of any other place in the United States that has the aptitude for the full range of spinal care that Mayo Clinic has.”

Figure 2. A. Lateral X-ray shows spinal deformity before surgery. B. Post-surgery lateral X-ray shows spinal alignment.
**Novel Biomarker for a Treatable Meningoencephalomyelitis**

Researchers at Mayo Clinic in Rochester, Minnesota, have identified an astrocytic autoantibody as a biomarker of relapsing autoimmune meningoencephalomyelitis. The antibody — which targets glial fibrillary acidic protein (GFAP) — has been found in more than 100 patients screened at Mayo Clinic.

“This is a new antibody, verifiable by all the stringent tests that we use,” says Vanda A. Lennon, M.D., Ph.D., a consultant in neuroimmunology at Mayo Clinic’s campus in Minnesota. “Although GFAP has been associated in the literature with other conditions, to date we find this GFAP antibody only in the spectrum of autoimmune meningoencephalomyelitis.”

“GFAP meningoencephalomyelitis is a rapidly progressive disorder and can be potentially devastating neurologically. However, it is exquisitely steroid responsive,” adds Andrew McKeon, M.B., B.Ch., M.D., an autoimmune neurologist at Mayo Clinic’s campus in Minnesota.

Prominent clinical manifestations of the condition include headache, subacute encephalopathy, optic papillitis, inflammatory myelitis, postural tremor and cerebellar ataxia. “Patients might have weakness, behavioral problems or forgetfulness,” Dr. Lennon says. The condition can be mistaken for meningeval tumor, multiple sclerosis, central nervous system vasculitis, central nervous system lymphoma or sarcoidosis.

A clinical test for the GFAP autoantibody is expected to be available from Mayo Clinic in autumn 2017. In the meantime, the Mayo Clinic Neuroimmunology Research Laboratory can accept patient samples of blood and cerebrospinal fluid (CSF) for testing, and report the results to referring physicians.

**Eminently treatable**

Since Dr. Lennon established the Neuroimmunology Laboratory 35 years ago, she and colleagues have conducted groundbreaking research on neural autoantibodies. The laboratory’s algorithm for neural-specific immunoglobulin G detection incorporates a mouse tissue-based immunofluorescence assay that reveals clinically pertinent autoantibodies.

“This assay has been an amazing discovery tool since the 1960s, when it was first described,” Dr. Lennon says. “Rather than developing a theory and then searching for an antibody that fits it, we put patient serum on sections of mouse tissues, see what binds, and then further investigate. Through this we’ve been discovering a series of very informative antibodies, which are then subjected to molecular confirmation.”

The novel GFAP autoantibody drew the researchers’ attention due to its unique staining pattern resembling astrocytes. The autoantibody was subsequently found in CSF and serum samples of 103 patients who underwent testing for potential autoimmune neurological disorders at Mayo Clinic. Retrospective review of medical records confirmed Dr. McKeon’s early observation that many of these seropositive patients were women with ovarian teratoma or women with encephalitis who subsequently developed ovarian teratoma.

In a study published in *JAMA Neurology*, the Mayo Clinic researchers focused on the initial 16 GFAP autoantibody positive cases. Their median age at neurological symptom onset was 42 years. CSF was inflammatory in 13 of 14 patients with data available. Neoplasia was diagnosed within three years of neurological onset in six of the 16 patients (38 percent).

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**Figure 1.** On the left, axial T2-weighted MRI of the head demonstrates diffuse T2-hyperintense signal within the white matter. On the right, T1-weighted post-gadolinium image shows the characteristic radial enhancement pattern.
Subthreshold Cortical Stimulation for Epilepsy

For patients with drug-resistant focal epilepsy, surgery is the most effective treatment. However, surgery isn’t feasible when seizures originate from the eloquent cortex. Focal brain stimulation has been shown to be efficacious, but typical approaches — such as vagal nerve stimulation or responsive nerve stimulation — rarely yield seizure-free outcomes.

Neurologists at Mayo Clinic in Rochester, Minnesota, have successfully suppressed seizures in patients treated with chronic subthreshold stimulation of the cortex. In a research letter published in *JAMA Neurology*, Mayo Clinic neurologists reported that 10 of 13 patients (76.9 percent) had improvement for epilepsy severity and quality of life after chronic subthreshold stimulation. The majority of patients experienced a reduction in seizure frequency of more than 50 percent and a pronounced reduction in interictal epileptiform discharges that occurred within minutes of initiating stimulation.

“This option will provide us with a plan B if we can’t do a surgical resection for a patient with focal epilepsy,” says Jeffrey W. Britton, M.D., a consultant in Neurology at Mayo Clinic’s campus in Minnesota. “Subthreshold cortical stimulation shows promise in allowing us to stop seizures in critical brain regions without affecting function.”

“Historically, we’ve thought about stimulation as a secondary alternative when surgery isn’t possible. But improving stimulation technology opens up a new therapeutic approach,” says Gregory A. Worrell, M.D., Ph.D., a consultant in Neurology at Mayo Clinic’s campus in Minnesota.

Stopping seizures before they start

Existing responsive neurostimulation devices detect abnormal electrical activity and then deliver electrical stimulation to normalize brain activity before the patient experiences a seizure. “By the time the responsive device detects abnormal electrical activity, it might be too late to prevent a seizure,” Dr. Britton says. “In contrast, subthreshold cortical stimulation tries to stun the brain before it goes into seizure — instead of catching the snowball, subthreshold stimulation can prevent it from ever starting down the hill.”

The subthreshold stimulation used at Mayo Clinic is a repurposed device approved for treatment of other neurological disorders. Initially, patients undergo several days of electroencephalographic monitoring with surgically implanted
electrodes. Once the seizure focus is pinpointed, patients are given a therapeutic trial of continuous subthreshold cortical stimulation. If the stimulation is clinically beneficial, the recording electrodes are replaced with permanent electrical contacts. Electrodes can be placed on or in the brain — at the precise location of seizure onset — and are connected to a generator implanted in the chest (Figure).

“The entire process can take a week or two, with patients usually in the hospital for seven to 20 days,” says Jamie J. Van Gompel, M.D., a consultant in Neurologic Surgery at Mayo Clinic’s campus in Minnesota.

None of the patients in the Mayo Clinic research has experienced adverse effects from the treatment. Four patients achieved cessation of their disabling seizures. Ten patients overall reported significant improvement in seizure intensity and duration.

**On his feet again**

Although patients treated with chronic subthreshold cortical stimulation aren’t always seizure-free, the impact of treatment can be life-changing. Dr. Van Gompel cites the case — described in the April 2016 issue of the *Journal of Neurology, Neurosurgery & Psychiatry* — of a man in his 20s who came to Mayo Clinic after being told elsewhere there were no options for treatment. The patient had previously undergone cortical resection, which stopped his day-to-day seizures. But he could no longer stand because doing so triggered seizures. As a result, he hadn’t walked in five years.

“We placed a grid in the appropriate brain area because we knew the seizures were happening in the legs,” Dr. Van Gompel says. “Then we asked him to stand, and we recorded the seizures. After proving that subthreshold stimulation allowed him to stand, we implanted chronic stimulation. A week later, he walked out of the hospital and went down to the mall.”

Another patient, who came to Mayo Clinic with epilepsy partialis continua, had experienced continued facial movements for four years. After treatment with chronic subthreshold stimulation, the patient has facial movements only when she becomes nervous.

“Her seizures are not entirely controlled, but she’s no longer having continual facial movements. It has been very helpful for her quality of life,” Dr. Van Gompel says.

Unlike anti-seizure medications, which have widespread effects on the brain, subthreshold cortical stimulation directs treatment at the precise area of seizure focus. “We’re bringing electricity right to the problem,” Dr. Van Gompel says.

“This therapy provides levels of electrical stimulation low enough to kind of stun part of the brain so it cannot generate a seizure, yet does not cause that part of the brain to be completely non-functional,” Dr. Britton adds. “We are cautiously optimistic we may have a long-term solution for these patients.”

**For more information**


Expertise for Complex Tumor Surgery in Florida

Surgery to remove brain and skull base tumors poses significant risks of morbidity, due to these tumors’ proximity to eloquent brain tissue or to important neurovascular structures, neural canals or the cavernous sinus. These procedures require the skills of a multidisciplinary team of specialist physicians, nurses and technicians. As a primary regional medical center in the southeastern United States, Mayo Clinic in Jacksonville, Florida, has the resources to handle these challenging cases.

“At Mayo Clinic we see patients with tumors that are extremely complex and dangerous, and often considered inoperable because of their location in eloquent brain or at the skull base. We can offer these patients the expertise of a medical team that focuses on these complex tumors,” says Alfredo Quinones-Hinojosa, M.D., chair of Neurosurgery at Mayo Clinic’s campus in Florida.

The surgical teams for these cases can include neurosurgeons, neurologists, otorhinolaryngologists, neuroanesthesiologists, plastic surgeons, neuro-ophthalmologists, oncologists, as well as nurses and technicians specializing in complex neurosurgery. “There might be a team of 20 to 30 people to take care of one patient, from when that patient walks through the door until he or she leaves the institution,” Dr. Quinones-Hinojosa says. “Very few centers in the United States have this team expertise. That is what makes Mayo Clinic so special.”

Synergy of practice and research

Dr. Quinones-Hinojosa’s clinical work at Mayo Clinic focuses on gliomas, pituitary adenomas, meningiomas and metastatic brain tumors. He and other neurosurgeons at Mayo Clinic’s campus in Florida have experience with awake craniotomies for patients with tumors in speech or motor areas of the brain, and with endoscopic removal of skull base tumors. Intraoperative monitoring to measure neural function and integrity is also an important aspect of complex neurosurgery at Mayo Clinic.

The clinical neurosurgery practice is fed by research. In addition to caring for patients, Dr. Quinones-Hinojosa directs the Mayo Clinic Neurosurgery Brain Tumor Stem Cell Laboratory. With patient consent, every neurological tumor removed from a patient at Mayo Clinic’s campus in Florida is preserved for research. Dr. Quinones-Hinojosa’s laboratory focuses on the study of cancer migration and progression in the brain and of invasive cell populations, in an effort to find novel therapeutic targets to affect tumor progression.

In a study published in the June 21, 2016, issue of Cell Reports, Dr. Quinones-Hinojosa and colleagues describe an experimental platform that analyzes patient samples at the single-cell level. The researchers used the platform to screen patient-derived glioblastoma samples, and observed that the migratory phenotype of a subset of cells in response to platelet-derived growth factor was highly predictive of tumor location and recurrence in the clinic (Figure).

“This has tremendous implications for the care of patients,” Dr. Quinones-Hinojosa says. “We are now at a point where we can design new methods and drugs to target the agents that drive cell migration. We are talking about a direct effect for the patient from laboratory research, but it all started with the patient.

“What makes Mayo Clinic so special,” he adds, “is that we are in the business of taking care of patients — of finding cures and giving patients hope.”

For more information

Research Highlights in Neurology and Neurosurgery

Hippocampal Volumes Predict Risk of Dementia With Lewy Bodies
Identifying patients with mild cognitive impairment (MCI) who are at risk of dementia with Lewy bodies (DLB) is critical for early interventions. However, correct diagnosis is complicated by the similarity of signs and symptoms of DLB and Alzheimer's disease (AD). Researchers at Mayo Clinic in Rochester, Minnesota, found that patients with MCI who have no hippocampal shrinkage were 5.8 times more likely to develop probable DLB than were patients with hippocampal atrophy, which is associated with AD. The study followed 160 patients with MCI who participated in an MRI study at baseline from 2005 to 2014. The study participants had annual clinical evaluations. During a median follow-up period of two years, 20 (13 percent) of the patients with MCI progressed to probable DLB, and 61 (38 percent) progressed to AD dementia. Seventeen of the 20 patients (85 percent) who developed probable DLB had a normal hippocampal volume; 37 of the 61 patients (61 percent) who developed AD had hippocampal atrophy. The relationship of hippocampal volume and disease was stronger among people with nonamnestic MCI. The researchers note that 49 percent of the 160 patients in the cohort were stable during follow-up but might progress to probable DLB or AD dementia in the future. (Kantarci K, et al. Hippocampal volumes predict risk of dementia with Lewy bodies in mild cognitive impairment. Neurology. 2016;87:2317.)

Progressive Solitary Sclerosis
Most patients with multiple sclerosis (MS) have either a relapsing-remitting course associated with inflammatory clinical attacks that usually resolve, or an insidiously progressive course with or without prior relapses. Disability typically accrues during the progressive course. However, a clinical-radiologic paradox exists, with an incomplete association between the number of MS demyelinating lesions and development of a progressive MS course. Although progressive motor impairment similar to progressive MS disease courses may occur from an isolated demyelinating lesion in the central nervous system (CNS), current criteria preclude a diagnosis of MS in such cases due to a failure to document dissemination in time and space. Researchers at Mayo Clinic in Rochester, Minnesota, have described 30 patients with what they call “progressive solitary sclerosis”: progressive motor impairment directly attributable to an isolated CNS demyelinating lesion in the spinal cord, brainstem or cerebral white matter. The researchers identified patients who had progressive motor impairment for more than one year, only a single radiologically identified CNS demyelinating lesion along corticospinal tracts and no history of relapses affecting other CNS pathways. Clinical presentations included hemiparesis, monoparesis, quadriparesis and paraparesis. Multiple brain and spinal cord MRIs were reviewed by a neuroradiologist blinded to the clinical details, over a median follow-up period of 100 months from symptom onset. In all cases the insidiously progressive motor neuron impairment was explained by the location of the solitary CNS demyelinating lesion. All patients’ progressive CNS disease was indistinguishable from patients with primary progressive MS or secondary progressive MS who fulfill current diagnostic criteria. The researchers suggest that future revisions of MS diagnostic criteria should consider accommodating this subtype of demyelinating disease. (Keegan BM, et al. Progressive solitary sclerosis: Gradual motor impairment from a single CNS demyelinating lesion. Neurology. 2016;87:1713.)

Single Recessive Gene Mutation Implicated in Early-Onset Parkinson’s Disease
Despite recent progress, the genetic contribution to Parkinson’s disease (PD) is not fully elucidated. It has been postulated that heterozygous mutations in recessive PD genes might increase the risk of developing the disease. In particular, the PTEN-induced putative kinase 1 (PINK1) p.G411S mutation has been reported in families with dominant inheritance patterns of PD, suggesting that it might confer a sizable disease risk when present on only one allele. Led by scientists from Mayo Clinic in Jacksonville, Florida, a collaboration of researchers in seven countries has established PINK1 p.G411S as a rare genetic risk factor with a relatively large effect size conferred by a partial dominant-negative function phenotype. The researchers examined families with the mutation and conducted a genetic association study with 2,560 patients with PD and 2,145 control subjects. Genetic analyses as well as functional, cell-based and structural computational characterizations were performed in the case-control study. The researchers found that the p.G411S mutation in a single allele substantially inhibits the protein produced by the healthy PINK1 allele, disrupting the process that removes damaged mitochondria from neurons. Among study participants with the PINK1 p.G411S mutation, the median age at disease onset was 59 years — significantly lower than age of disease onset in noncarriers. (Puschmann A, et al. Heterozygous PINK1 p.G411S increases risk of Parkinson’s disease via a dominant-negative mechanism. Brain. 2017;140:98.)

To read more about Mayo Clinic neurosciences research and patient care, visit http://www.mayoclinic.org /medical-professionals.
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