

Neurosciences Update

Neurosciences News From Mayo Clinic Vol. 19, No. 1, 2022

JANUARY 2022

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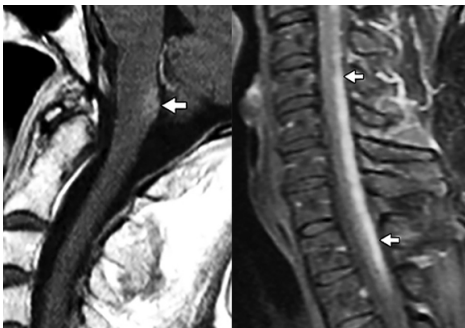


Figure. On the left, MRI shows lesions in the AQP4-enriched postrema, characteristic of some patients with NMOSD. On the right, MRI of a patient with sarcoidosis illustrates the differing imaging characteristics of the two conditions.

Neuromyelitis Optica: New Therapies Offer Hope

The Food and Drug Administration (FDA) has approved the use of three medications for the treatment of neuromyelitis optica spectrum disorder (NMOSD). Mayo Clinic led the biomarker discovery and subsequent epidemiologic, immunopathological, clinical and radiologic phenotyping of this debilitating inflammatory central nervous system disorder.

“NMOSD is considered an orphan disease. The fact that we have three FDA-approved drugs within a year of one another is pretty incredible,” says Sean J. Pittock, M.D., an autoimmune neurologist who directs the Neuroimmunology Research Laboratory and the Center for Multiple Sclerosis and Autoimmune Neurology at Mayo Clinic in Rochester, Minnesota.

NMOSD manifests primarily as relapsing episodes of severe optic neuritis and longitudinally extensive transverse myelitis (Figure). Historically misdiagnosed as multiple sclerosis, NMOSD is characterized by more-severe attacks and less complete recovery. The median age of onset is 35 to 37 years.

“There’s always a possibility that an attack could leave the person with a deficit such as blindness in an eye or difficulty walking,” says Dean M. Wingerchuk, M.D., an autoimmune neurologist at Mayo Clinic in Phoenix/Scottsdale, Arizona. “The attacks

are also very unpredictable. Patients always live with the specter of drastic change that could happen to them quickly.”

Unlike multiple sclerosis, in which morbidity generally accrues as part of the disease’s disability phase, NMOSD has cumulative effects. “Each NMOSD attack leads to additional disability for most patients,” says Alfonso (Sebastian) S. Lopez Chiriboga, M.D., an autoimmune neurologist at Mayo Clinic in Jacksonville, Florida. “In rare instances, when severe inflammation causes upper cervical cord lesions, patients can succumb to respiratory failure.”

NMOSD has traditionally been treated with immunosuppressants. However, controlled studies have been lacking, and up to half of patients continue to experience attacks while receiving these therapies. The newly approved treatments are three monoclonal antibodies:

- Eculizumab, a complement inhibitor
- Inebilizumab, an anti-CD19 agent
- Satralizumab, an anti-interleukin-6 receptor

“They’re all excellent therapies. They’re also quite different from one another in some respects,” Dr. Wingerchuk says. “Our neurologists have seen hundreds of people with NMOSD. That experience is very helpful in counseling patients about treatment.”



Sean J. Pittock, M.D.

Mayo Clinic has pioneered the research and clinical management of NMOSD for more than 20 years. The discovery of an antibody biomarker by a team led by Vanda A. Lennon, M.D., Ph.D., an immunologist at Mayo Clinic in Minnesota, revolutionized the diagnosis and treatment of NMOSD.

Subsequent studies of the antibody — known as neuromyelitis optica antibody (NMO-IgG) — and its target, the aquaporin-4 (AQP4) water channel, facilitated improved understanding of the immunopathological mechanisms underlying the disorder and allowed the development of novel therapies. Although considered rare, AQP4-IgG-seropositive NMOSD affects about half a million people worldwide, disproportionately women and people of color.



Dean M. Wingerchuk, M.D.

Drs. Pittock and Wingerchuk led a Mayo Clinic trial of eculizumab, published in *The Lancet* in 2013, that demonstrated nearly complete cessation of disease activity in patients severely affected by NMOSD, paving the way for eculizumab’s phase 3 clinical trial. In addition, Drs. Pittock and Wingerchuk served with Brian G. Weinschenker, M.D., a neurologist at Mayo Clinic’s campus in Minnesota, on the steering committee of the clinical trial investigating inebilizumab for the treatment of NMOSD.

“The fact that we now have three medications that target the specific disease pathways in patients with the aquaporin-4 antibody is a game changer,” Dr. Lopez Chiriboga says.



Alfonso (Sebastian) S. Lopez Chiriboga, M.D.

THERAPEUTIC DECISION-MAKING

None of the newly approved treatments caused major side effects among trial participants. Beyond that, direct comparison of the clinical trial results is difficult due to the trials’ differing designs and definitions.

Mayo Clinic autoimmune neurologists advise physicians and patients to consider each therapy’s efficacy, convenience and cost:

- In the PREVENT eculizumab trial, published in *The New England Journal of Medicine* in 2019, 98% of patients receiving the therapy were relapse-free 144 weeks after starting treatment, com-

pared with 45% in the placebo group. Eculizumab must be infused at a medical center every two weeks and costs about \$710,000 a year.

- In the N-MOmentum inebilizumab trial, published in *The Lancet* in 2019, 88% of patients receiving the therapy were relapse-free 28 weeks after starting treatment, compared with 61% in the placebo group. Inebilizumab must be infused at a medical center every six months. It costs \$393,000 the first year and \$262,000 a year after that.
- In the SAKuraStar/SAKuraSky satralizumab trials, published in *The New England Journal of Medicine* in 2019 and *The Lancet* in 2020, approximately 78% of patients receiving the therapy were relapse-free 96 weeks after starting treatment, compared with 59% in the placebo group. Satralizumab is injected under the skin at home once a month. It costs \$219,000 the first year and \$190,000 a year after that.

Rituximab, a monoclonal antibody often used to treat NMOSD, costs about \$18,000 a year. The cost continues to decline, as the medication is now off patent. Regulatory approval hasn’t been sought for rituximab as an NMOSD treatment.

Dr. Pittock notes that a recent randomized controlled trial at a single institution in Japan found that rituximab was more effective than a placebo. Although the study’s small size precludes meaningful quantification of risk, “it’s difficult to ignore rituximab,” Dr. Pittock says.

Mayo Clinic is currently a site for a pharmaceutical company-funded study investigating ravulizumab, a monoclonal antibody inhibitor of complement activation that is similar to eculizumab but with a longer half-life. “Potentially, this therapy would need to be given only every eight weeks,” Dr. Pittock says.

Mayo Clinic’s leadership in complex diseases such as NMOSD stems from a commitment to innovation. In addition to laboratory studies of the disease’s underlying mechanisms, diagnostic assays are developed through Mayo Clinic Laboratories. The positive predictive value for Mayo’s NMO/AQP4-IgG assays is 100%.

The Mayo Clinic Neuroimmunology Research Laboratory discovers approximately two new antibody biomarkers of autoimmune or paraneoplastic neurological disorders a year. “We are making giant leaps in moving the field of autoimmune neurology forward. This allows us to provide molecular target-based diagnoses, which opens up the field for personalized targeted immunotherapies,” Dr. Pittock says.

“At Mayo Clinic, our work goes from bench to bedside — from biomarker discovery to treatments that can stop attacks,” he adds. “By stopping NMOSD attacks, we can potentially stop the accrual of disability.”

FOR MORE INFORMATION

Center for Multiple Sclerosis and Autoimmune Neurology. Mayo Clinic. <https://www.mayo.edu/research/centers-programs/center-multiple-sclerosis-autoimmune-neurology/overview>.

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Yamamura T, et al. Trial of satralizumab in neuromyelitis optica spectrum disorder. *The New England Journal of Medicine*. 2019;381:2114.

Traboulsee A, et al. Safety and efficacy of satralizumab monotherapy in neuromyelitis optica spectrum disorder: A randomised, double-blind, multicentre, placebo-controlled phase 3 trial. *The Lancet*. 2020;19:402.

Precise and Personalized Guidance for Epilepsy’s Complex Decisions

Approximately one-third of people with epilepsy have medically refractory seizures. Those patients, and their physicians, face complex decisions about treatment. Mayo Clinic takes an individualized approach, with comprehensive testing to determine each person’s optimal treatment.

“Each patient has a unique epilepsy network that must be closely scrutinized. That means every person needs his or her own set of tests,” says Cornelia N. Drees, M.D., an epileptologist at Mayo Clinic in Phoenix/Scottsdale, Arizona. “The testing data are then interpreted by a multidisciplinary team that comes to a consensus tailored to that patient.”

Patient education is an important part of the process. Mayo Clinic epileptologists take time to explain the treatment options and to discuss each individual’s support system.

“Epilepsy monitoring and treatment can be frightening for patients. Many variables need to be addressed,” Dr. Drees says. “Treatment will always be focused on making a person seizure-free, but sometimes that’s difficult. Beyond trying to cure epilepsy, one important goal is always to improve a person’s quality of life, given the constraints of an individual’s condition.”

MULTIPLE TREATMENT OPTIONS

Once an individual’s epilepsy hasn’t responded to two medications, each additional medication that is tried has a less than 5% chance of making that person seizure-free. Mayo Clinic uses sophisticated testing to help determine the optimal surgical treatment approach.

In addition to inpatient video-electroencephalography epilepsy monitoring, testing might include subtraction ictal SPECT coregistered to MRI (Figure, see page 4), CT, MRI or positron emission tomography. “The



Cornelia N. Drees, M.D.

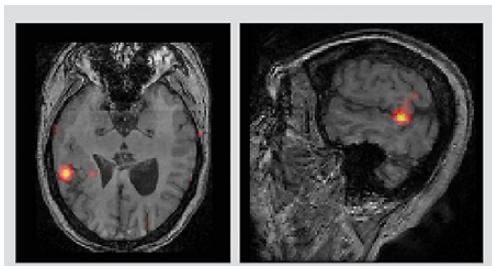


Figure. Subtraction ictal SPECT coregistered to MRI images pinpoint seizure focus.

evaluation of these patients is a multistep process,” Dr. Drees says. “We work closely with our neuroradiologists and neuropsychologists to obtain the information we need to recommend treatment.”

The resection, laser ablation or disconnection of a seizure focus can make a person seizure-free. When that isn’t possible, nonmedical treatment options at Mayo Clinic include a ketogenic diet, which can significantly lower seizure frequency.

Several stimulation devices, most surgically implanted, also are available, including vagus nerve stimulation, responsive neurostimulation, chronic subthreshold cortical stimulation, deep brain stimulation and transcranial magnetic stimulation. “These devices are palliative. They are more likely to reduce seizures than to stop them,” Dr. Drees says.

“Surgical resection of brain areas that are causing seizures is likelier to lead to cure.”

The multidisciplinary team that guides patients through the treatment process includes a neuropsychologist and a social worker, when needed. “Before and even after any procedure, many of our patients need help — with their family dynamics, with transportation, with finishing education or having job training,” Dr. Drees says. “In addition to giving medical care, an epilepsy team can provide companionship and expertise to help maximize the quality of life.”

All too often, patients are reluctant to seek surgical treatment for epilepsy. “That hesitancy can be overcome with education,” Dr. Drees says. “We can help people understand that there are many options to consider.”

Comprehensive Mapping of Cognitive Functions During Awake Surgery

Mayo Clinic uses innovative technology to map patients’ cognitive functions during awake brain surgeries. The latest tool is NeuroMapper, a tablet-based testing platform developed by David S. Sabsevitz, Ph.D., initially at the Medical College of Wisconsin in collaboration with the University of Wisconsin-Milwaukee, and with continued development at Mayo Clinic in Jacksonville, Florida. Dr. Sabsevitz is currently a neuropsychologist at Mayo’s Jacksonville campus, where NeuroMapper has been used in more than 200 surgeries.



David S. Sabsevitz, Ph.D.

“In the past, we have relied on very simplistic and inefficient brain-mapping methods in the operating room. More detailed and sophisticated evaluation of patients is needed to truly capture the variability in the locations of individuals’ brain functions and avoid resecting functionally important tissue,” Dr. Sabsevitz says. “Advanced imaging and mapping translate to better surgical outcomes.”

The NeuroMapper platform comprises a tablet attached to the operating room table, which the patient can see and interact with, and another tablet used by a neuropsychologist (Figure, see page 5) to select tests for

the patient to perform. The neuropsychologist’s tablet displays and tracks the patient’s test results.

The platform contains comprehensive, conceptually informed language tests that measure not just the ability to name a picture but also a wide range of other linguistic functions that are at risk during surgery. In addition, NeuroMapper contains paradigms that allow for the mapping of nonlanguage functions, such as attention, higher level problem-solving and multitasking.

“The platform captures a great deal of information and displays it to the examiner in real time,” Dr. Sabsevitz says. “We can monitor brain functions with increased sensitivity and use that information for clinical decision-making. As a result, our cohesive, multidisciplinary team is able to attempt high-risk resections for the treatment of epilepsy or brain tumor.”

A multidisciplinary approach is key to awake brain surgery. In addition to including neuropsychologists, Mayo Clinic’s treatment team involves neurosurgeons, neurologists, neuro-anesthesiologists and neuroradiologists.

“NeuroMapper combines innovative technologies in a highly collaborative environment to address very complex medical problems,” says William V. Bobo, M.D., M.P.H., chair of Psychiatry and Psychology at Mayo Clinic’s campus in Jacksonville, Florida. “More than that, the platform enables our neuroscience colleagues to offer something truly unique that enhances the care of patients.”

SYSTEMIZING BRAIN MAPPING

At Mayo Clinic, patients undergo detailed neuropsychological assessments before awake brain surgeries. Functional MRI and diffusion tensor imaging are routinely used for pre-surgical brain mapping.

“Our radiology department has extensive experience in functional brain mapping and advanced structural imaging,” Dr. Sabsevitz says. “Everything we do in the pre-surgical work-up and in the operating room is designed to minimize morbidity.”

During surgery, a patient’s reaction times can be compared to the results of that individual’s pre-surgical testing. “If the patient’s accuracy drops or responses are slowing down, we can alert the surgeon,” Dr. Sabsevitz says.

As described in a video article published in the September 2020 issue of *World Neurosurgery*, NeuroMapper allows the surgical team to efficiently collect comprehensive information. “We can do much more extensive testing in a given timespan,” Dr. Sabsevitz says. “Before we had this platform, it was very hard to keep track of all this information.”

NeuroMapper is currently used at approximately 25 institutions across the United States. Mayo Clinic is organizing a research consortium of platform users to collect data and to better systemize brain mapping.

Point-of-Care Additive Manufacturing Provides Complex Scoliosis Models

Mayo Clinic has the largest point-of-care additive manufacturing facility in the United States. The 8,000-square-foot space provides highly accurate 3D-printed anatomic models and surgical guides for

“The approach to brain mapping has been incredibly variable across institutions,” Dr. Sabsevitz says. “Our hope is that by introducing a more structured mapping platform, we can pool NeuroMapper data across institutions to answer very complex research questions that accelerate our understanding of the brain and improve surgical techniques.”

Mayo Clinic is also working to integrate the mapping of sensory motor systems into the platform. Testing is underway on devices that would objectively and precisely measure a patient’s strength and speed of movement while simultaneously testing functions such as language and attention.

“NeuroMapper could alert us if a patient is getting weaker while interacting with the device,” Dr. Sabsevitz says.

As a high-volume center for awake brain surgery, Mayo Clinic also works to educate patients about the procedure. “Being told that you need to have an awake brain surgery is incredibly stressful. At Mayo, we spend a lot of time preparing our patients and their families for these procedures through supportive counseling and education,” Dr. Sabsevitz says. “The feedback we get from patients is that we turned a potentially scary and traumatic situation into something quite doable.”

FOR MORE INFORMATION

Medical College of Wisconsin.
<https://www.mcw.edu>

University of Wisconsin-Milwaukee.
<https://uwm.edu>

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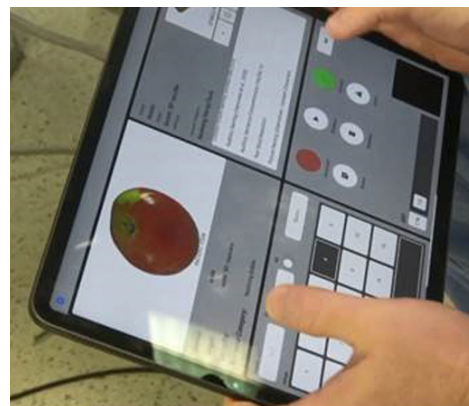


Figure. Intraoperative photograph shows the NeuroMapper platform on tablets used simultaneously by a neuropsychologist and a patient.



William V. Bobo, M.D., M.P.H.



Figure. Jeremy L. Fogelson, M.D., a neurosurgeon specializing in spinal care at Mayo Clinic in Rochester, Minnesota, examines a 3D-printed spinal model in the operating room.



Jonathan M. Morris, M.D.



Jeremy L. Fogelson, M.D.

customized CT and MRI protocols to the creation of a patient-specific, life-sized 3D-printed models or devices,” says Jonathan M. Morris, M.D., a neuroradiologist and medical director of the 3D Anatomic Modeling Laboratory at Mayo Clinic in Rochester, Minnesota.

The models are valuable pre-surgical and intraoperative tools for the treatment of adults with complex scoliosis (Figure). “Holding a 3D model makes it much easier to understand complex anatomy, particularly in revision surgeries or in patients with congenital adult scoliosis,” says Jeremy L. Fogelson, M.D., a neurosurgeon specializing in spinal care at Mayo Clinic in Rochester, Minnesota. “When we look at 2D images on a screen, we see one slice at a time and then have to do a lot of mental juggling to reconstruct those slices into a real-life image.”

Dr. Fogelson cites a case in which a 3D spinal model indicated that an adult scoliosis surgery would be more complex than he initially thought. “The patient was a man with very large bones. An X-ray can’t show you bone size,” Dr. Fogelson says. “But when I held the model, I realized we needed to operate over two days in order to safely work through that much tissue.”

Mayo’s model-manufacturing process starts with CT and sometimes volumetric MRI, using imaging protocols designed by Mayo Clinic radiologists specifically for 3D printing. A Mayo radiologist evaluates the accuracy of the imaging data before the model is produced.

“Our patient-specific models aren’t developed only according to an algorithm created by an engineer who doesn’t fully understand anatomy,” Dr. Morris says. “The biomedical engineers in our facility are part of the clinical care team, routinely working with radiologists and surgeons.”

The imaging data are segmented, and the model is created using several 3D printers. “No single printer does it all — we have the capability to do additive manufacturing using all seven ASTM standards,” Dr. Morris

says. “The life-sized model we give to the surgeon is exactly what the surgeon is going to find during the patient’s procedure.” Mayo Clinic launched its additive manufacturing facility in 2005. Mayo’s campuses in Arizona and Florida also have 3D anatomic modeling laboratories as of 2020, with collaboration occurring enterprisewide.

As a tertiary center, Mayo Clinic performs a high volume of revision surgeries for adults with complex scoliosis. The 3D imaging protocols use advanced techniques such as iterative metal artifact reduction and multispectral energy to reduce artifacts from metal implants. “Without those techniques, we don’t get an accurate model,” Dr. Morris says.

The 3D models can enhance the safety of revision procedures, which are often performed in the absence of anatomic landmarks removed during the patient’s original procedure. “It can be challenging to determine optimal screw placement in a revision spine with bone grafts,” Dr. Fogelson says. “Examining the 3D model before surgery — rotating it and looking at the side of the spine that will remain covered during the surgery — guides our screw locations and trajectories. We also save time in the operating room because at times we don’t need additional imaging or technology to guide screw placement.”

Mayo Clinic performs 3D printing in numerous materials, including sterilizable materials for use in the operating room. Planning is underway for printing on titanium through Mayo Clinic Engineering.

“That will allow us to innovate and serve more patients with unique needs,” Dr. Morris says. “Our goal is to provide complex, customizable models and guides that benefit our patients, who come to Mayo for solutions they can’t get anywhere else.”

FOR MORE INFORMATION

3D Anatomic Modeling Laboratories. Mayo Clinic. <https://www.mayoclinic.org/departments-centers/anatomic-modeling-laboratories/overview/ovc-20473121>.

Research Highlights in Neurology and Neurosurgery

INSIGHTS INTO THE CLINICAL RELEVANCE OF MS IMMUNOPATTERNS

Three distinct, commonly observed forms of the acute multiple sclerosis (MS) plaque have been described. These immunopatterns differ in the effector mechanism of demyelination. Mayo Clinic researchers have demonstrated that all three immunopatterns can be detected in active demyelinating lesions throughout the course of the disease, although with lower frequency later in the disease course. The researchers performed immunopathological subtyping on specimens from 547 patients with central nervous system demyelination confirmed with biopsy or autopsy or both. The researchers found that each patient expressed a single immunopattern across multiple active lesions obtained from serial biopsies or within a single autopsy. Among the other findings:

- Pattern 1 was identified in 23% of patients, pattern 2 in 56% and pattern 3 in 22%
- Pattern 3 was associated with a more fulminant initial attack compared with pattern 1 or pattern 2
- Patients with pattern 3 were overrepresented in the autopsy-only subgroup
- Index attack-related disability was higher in patients with pattern 3 than in patients with pattern 2
- Monophasic clinical course and progressive disease were more common in patients with pattern 3 than in patients with pattern 1 or 2
- Biopsied patients — who were likelier to have survived the initial attack — appear to have similar long-term outcomes regardless of immunopattern, suggesting convergence into a final common pathway related to the chronically denuded axon

The researchers note that the heterogenous immunopatterns detected in the early active plaque of people with MS suggest that tailored initial treatment enhances attack recovery or prevents the onset of secondary progressive disease. (Tobin WO, et al. Clinical correlation of multiple sclerosis immunopathologic subtypes. *Neurology*. 2021;97:e1906.)

THROMBECTOMY MODEL CAPTURES ARTERY-CLOT-DEVICE INTERACTION

The persistent challenges in thrombectomy for large-vessel occlusion, such as suboptimal complete recanalization and first-pass effect, imply an insufficient understanding of the artery-clot-device interaction. Mayo Clinic researchers have created a thrombectomy model that can capture that interaction through concurrent transmural and angiographic visualizations. The researchers collected fresh, nonfrozen whole human brain specimens and connected them to a customized pump system tuned to deliver saline flow at a physiologic flow rate and pressure. Angiography was performed to verify the flow in the anterior-posterior and vertebrobasilar circulations and collaterals. Large-vessel occlusion was simulated by embolizing a radiopaque clot analog. Thrombectomy was tested, and the artery-clot-device interactions were recorded by transmural and angiographic videos. The researchers found that baseline cerebral angiography revealed excellent penetration of contrast in the anterior-posterior and vertebrobasilar circulations without notable arterial cutoffs and with robust collaterals. Small branches and perforating arteries were consistently opacified with good patency. Three device passes were performed to achieve recanalization, with failure modes including elongation, fragmentation and distal embolization. The model provides critical insights into the action mechanism and failure modes of current and upcoming thrombectomy devices. (Liu Y, et al. A thrombectomy model based on ex vivo whole human brains. *American Journal of Neuroradiology*. 2021;42:1968.)

PROTOCOL TO CONTROL BLEEDING DURING PITUITARY ADENOMA RESECTION

Primary resection of adrenocorticotropic hormone (ACTH)-secreting pituitary adenoma has become standard-of-care treatment for Cushing disease. However, the surgery can be challenging due to the risk of intraoperative bleeding. Although tranexamic acid (TXA) is a widely used intravenous hemostatic, its potential benefit during resection of ACTH-secreting pituitary adenoma hasn't been studied. Mayo Clinic researchers have found that perioperative TXA represents a potentially efficacious approach to control bleeding during the procedure. The researchers devised a protocol for the administration of TXA to patients undergoing endoscopic endonasal approach for resection of ACTH-secreting pituitary adenoma. The protocol includes strict criteria defined by a patient's age, medical history and risk factors. Thirty patients who met the criteria had TXA 30 minutes before incision, followed by a maintenance infusion throughout the procedure. No incidence of myocardial infarction or postoperative thromboembolic event was noted. Subjective assessments indicated satisfaction with the patient selection protocol and meaningful reduction in the extent of intraoperative bleeding. The researchers note that formal testing in a randomized, controlled setting is needed. (Graffeo CS, et al. Perioperative tranexamic acid for ACTH-secreting pituitary adenomas: Implementation protocol results and trial prospectus. *World Neurosurgery*. 2021;153:e359.)

Education Opportunities

For more information or to register, visit <https://ce.mayo.edu/neurology-and-neurologic-surgery>, call 800-323-2688 or email cme@mayo.edu.

JUNE

Mayo Clinic Open and Endoscopic Techniques in Cranial Base Course

June 1-4, 2022

Mayo Clinic, Rochester, Minn.

JULY

Neurology in Clinical Practice 2022

July 14-17, 2022

Lowe's Coronado Bay Resort, Coronado, Calif.

5th Annual Mayo Clinic Advances and Innovations in Complex Neuroscience Patient Care: Brain and Spine 2022

July 27-30, 2022

Enchantment Resort Sedona, Sedona, Ariz.

NOVEMBER

Parkinson's Disease and Other Movement Disorders 2022

Nov. 4-5, 2022

Arizona State University (ASU) Health Futures Center, Phoenix

Neuroradiology: Practice to Innovation 2022

Nov. 7-11, 2022

The Ritz-Carlton, Grand Cayman, Grand Cayman, Cayman Islands

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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:

- Cerebral aneurysms
- Cerebral or spinal arteriovenous malformations
- Brain, spinal cord or peripheral nerve tumors
- Epilepsy with indications for surgery
- Carotid disease



Contact Us

Mayo Clinic welcomes inquiries and referrals, and a request to a specific physician is not required to refer a patient.

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Jacksonville, Florida

888-508-9912

Rochester, Minnesota

844-627-7684



Resources

[MayoClinic.org/medical-professionals](https://www.mayoclinic.org/medical-professionals)

Clinical trials, CME, Grand Rounds, scientific videos and online referrals

Neurosciences Update

Mayo Clinic Neurosciences Update is written for physicians and should be relied upon for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

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