

INSIDE THIS ISSUE

- 3 The Utility of Autonomic Testing
- 6 Mayo Clinic, Jacksonville, Florida, Brings Intraoperative MRI to the Region

Radiosurgery: An Effective Treatment for Benign Intracranial Tumors

Benign intracranial tumors occur about as often as primary malignant brain tumors. Most benign tumors are noninvasive, well defined, and well visualized on MRI and have a slow rate of progression. Each of these features makes them good candidates for radiosurgery—the single-session, focused delivery of radiation to an image-defined intracranial target.

The advantages of radiosurgery are that it can deliver a destructive dose of radiation to the target with little or no radiation effects on adjacent structures and that it is conducted in a single session. Having performed radiosurgery for the past 2 decades, Mayo Clinic neurosurgeons have accumulated a depth of expertise and a vast database that includes

patient characteristics, radiosurgical dosimetry, and outcomes. Mayo Clinic in Rochester, Minnesota, alone has conducted 4,500 procedures, 35% of which have been for benign tumors of one of the following types: meningiomas, vestibular schwannomas, or pituitary adenomas. For these types of tumors, control has been achieved in 95% of treated patients.

Bruce E. Pollock, MD, a Mayo Clinic neurosurgeon in Rochester, notes that proper patient selection is critical. Across Mayo Clinic's 3 sites in Arizona, Florida, and Minnesota, patients are seen by neurosurgeons who have expertise in both open procedures and radiosurgery. Having recently reviewed more than 1,400 cases of meningiomas, vestibular schwannomas, and pituitary adenomas, Dr

Pollock states that “when these

types of benign tumors are small, occur in critical locations, have atypical or malignant features, or have recurred following previous surgery, radiosurgery is an excellent choice.”

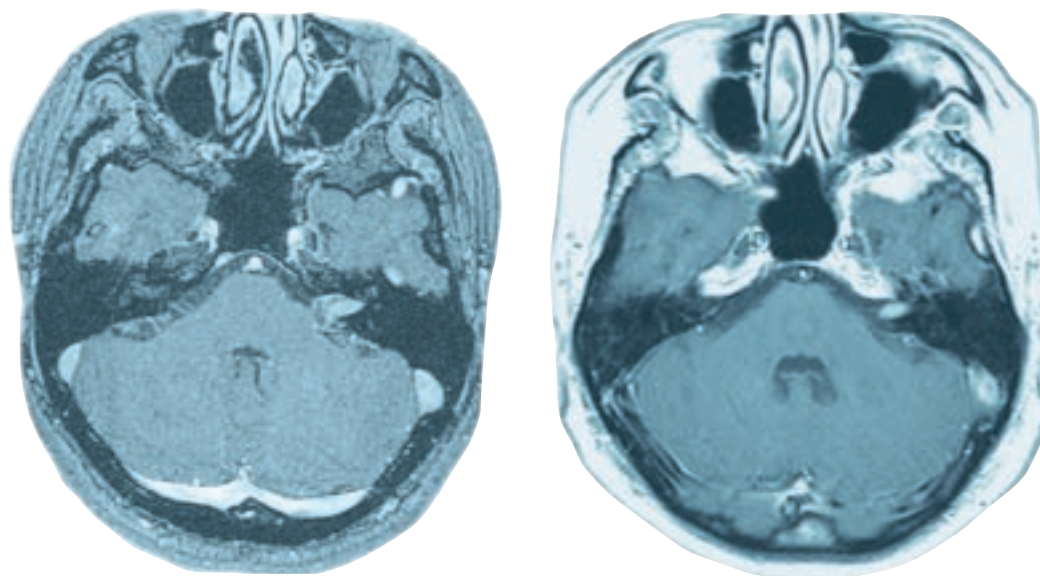


Figure 1. A patient with a vestibular schwannoma before radiosurgery (left, December 1997) and almost 12 years later (right, March 2009).



Bruce E. Pollock, MD

Mark K. Lyons, MD, a neurosurgeon at Mayo Clinic in Phoenix/Scottsdale, Arizona, adds that radiosurgery is well tolerated and of particular utility in elderly patients with medical conditions that put them at risk for an open procedure. He goes on to note that radiosurgery does not preclude an open procedure should that be necessary at a later time. For that reason, when given the option, many patients, regardless of age, choose radiosurgery to minimize the risk associated with open procedures.



Mark K. Lyons, MD

Radiosurgery for Meningiomas

Studies have found that the rate of recurrence for a surgically removed meningioma is about 18% to 25% at 10 years. As Ronald Reimer, MD, a Mayo Clinic neurosurgeon in Jacksonville, Florida, notes, “We’ve learned the importance of maintaining surveillance of meningiomas for a long period of time because they may recur or progress after many years of radiographic stability.” Radiosurgery has been found to reduce the risk of recurrence or progression. The 2 factors affecting both long- and short-term outcomes are tumor progression outside the field of radiation and tumor histology. Tumors that can be clearly imaged and those that are benign and without atypical histology have a far greater rate of success—progression-free survival at 5 years as high as 100% in a series of 206 tumors at Mayo Clinic compared with 83% for patients with atypical meningiomas.

Relative to brain site location Mayo clinicians have found that radiosurgery is an effective therapy for cavernous sinus meningiomas except when there is symptomatic mass effect, an unusual clinical presentation, or nontypical features on imaging. Radiosurgery is typically not recommended for convexity and parasagittal meningiomas.

Radiosurgery for Vestibular Schwannomas

Radiosurgery for small to moderate-sized vestibular schwannomas has been reported in several studies to improve the preservation of hearing and facial nerve function compared with surgical resection. This conclusion was supported by a Mayo Clinic study that compared surgical resection and radiosurgery for vestibular schwannomas with an average diameter of less than 3 cm. These Mayo investigators also found that the radiosurgical

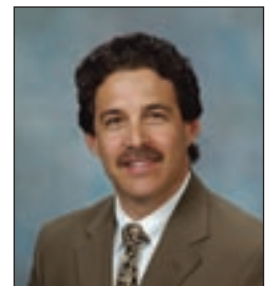
patients experienced less postprocedure dizziness. The Figure on page 1 shows images of a vestibular schwannoma in a patient before and almost 12 years after treatment with radiosurgery.

Radiosurgery for Pituitary Adenomas

Radiosurgery is considered safe and effective for hormone-secreting pituitary adenomas. A major advantage of radiosurgery for these tumors compared with radiotherapy is that radiosurgery appears to shorten by more than half the time to achieve biochemical remission and normalize hormone levels. Controversy remains over whether pituitary suppressive medications at the time of surgery have a negative impact on tumor control. However, several studies, including a series of 46 acromegaly cases at Mayo Clinic, found that patients were more than 4 times as likely to reach normal hormone levels if they were off such medications before surgery.

Dr Pollock notes that at Mayo Clinic patients with a pituitary adenoma that is both clearly defined and does not involve the optic apparatus are most often treated with radiosurgery. However, patients in whom a pituitary tumor appears to be enlarging and who experience new or progressing visual field deficits are referred for surgical resection. “Small pituitary adenomas can often be treated successfully with surgery, but those that extend beyond the confines of the pituitary fossa and extend up toward the optic nerves or hypothalamus can be more difficult to remove entirely at surgery,” notes Dr Reimer. A retrospective Mayo Clinic study of 62 patients with nonfunctional adenomas, 59 of whom had had prior tumor resection, found that with radiosurgery, the risk of new anterior pituitary deficits was 35% and that no patients experienced a decline in visual function.

Across Mayo’s 3 sites, neurosurgeons have found that as an alternative to or in conjunction with traditional neurosurgery, radiosurgery is an effective, noninvasive option for treating benign intracranial tumors.



Ronald Reimer, MD

The Utility of Autonomic Testing

Syncope, flushing, bladder and bowel dysfunction, dizziness, endocrine dysfunction, Parkinson-like symptoms, gastrointestinal tract distress, painful feet, orthostatic intolerance, extreme fatigue, tachycardia, cognitive dysfunction, anhidrosis, and hyperhidrosis—these are some of the symptoms and conditions that can benefit from autonomic testing. Referrals for autonomic evaluation across Mayo Clinic’s 3 sites are increasingly coming from outside the field of neurology as well as from within it. The growing number of referrals from disciplines such as cardiology, endocrinology, dermatology, gastroenterology, internal medicine, and urology may be a function of wider appreciation for the utility of autonomic testing for differential diagnosis and management.

In the 27 years since he founded the

autonomic testing laboratory at Mayo Clinic in Rochester, Minnesota, neurologist Phillip A. Low, MD, and his colleagues have established the norms and national standards for quantified evaluation of autonomic function. In the late 1990s, through the American Academy of Neurology, they generated the CPT codes for reimbursement. In conjunction with the thermoregulatory sweat test (TST), under the direction of fellow neurologist Robert D. Fealey, MD, since 1980, a strong battery of autonomic tests has been available at Mayo Clinic in Rochester for many years.

Routine reimbursable autonomic evaluation includes tests of sudomotor, cardiovagal, and adrenergic function. The tests are noninvasive. Because test results are quantifiable, responses from the 3 systems can be compared to determine selective and/or relative autonomic

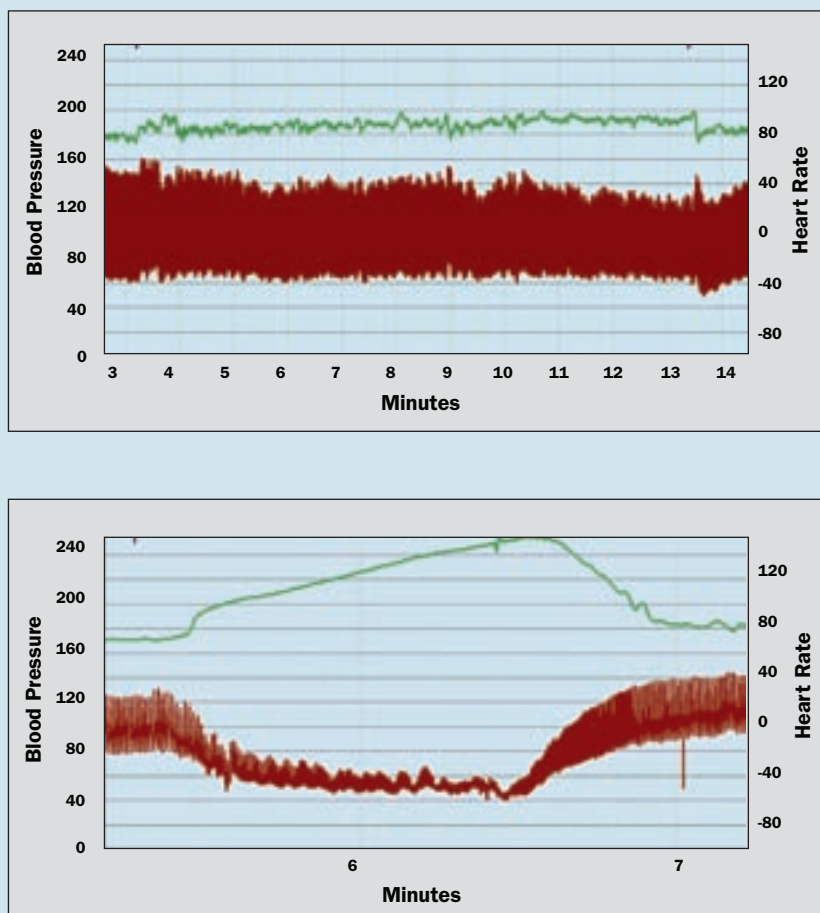


Figure. A graphic display of changes in blood pressure and heart rate (green line) over time in response to head-up tilt in a normal subject (top) and a patient with orthostatic hypotension.



Paola Sandroni, MD, PhD, and Phillip A. Low, MD

dysfunction. For example, a patient might have moderate involvement of the cardiovascular system and severe involvement of adrenergic function without impacting sudomotor function. Or both the cardiovascular and adrenergic systems may be normal in the face of isolated anhidrosis, suggesting the possibility of chronic idiopathic anhidrosis, a more benign disorder that does not progress to widespread autonomic failure and for which symptomatic and sometimes specific treatment is available. Only by testing all 3 systems can such diagnostically informative patterns emerge.

Autonomic testing helps to determine the presence, severity, distribution, and localization of autonomic dysfunction. It can distinguish primary from secondary autonomic disorders, true autonomic neuropathy from conditions that mimic it, and psychogenic from organic conditions. It can help to differentiate progressive diseases and serve as a means of monitoring disease progression and response to treatment. As an example, recent evidence from studies by Paola Sandroni, MD, PhD, a neurologist specializing in autonomic dysfunction at Mayo Clinic in Rochester, Dr Low, and their colleagues demonstrates that combined and detailed autonomic tests of symptoms and severity can distinguish multiple system atrophy from Parkinson disease (PD) and from PD with autonomic failure. Although autonomic disturbance is common in PD, its severity is more variable in PD than in multiple system atrophy, which is characterized by generalized autonomic failure affecting blood pressure, thermoregulatory sweating, bladder and erectile function, as well as cerebellar, extrapyramidal, and corticospinal function. Without autonomic testing, it can be difficult to distinguish the 2 diseases, a distinction that has major consequences for prognosis and management.

Routine Tests of Autonomic Function

Sudomotor Tests

The quantitative sudomotor axon reflex test (QSART) is used to evaluate postganglionic sudomotor function. The TST is used to evaluate both preganglionic and postganglionic function over the entire anterior body surface. When evaluated together in the same patient, TST and QSART can differentiate preganglionic from postganglionic lesions. For QSART, a stimulus solution of acetylcholine is applied using iontophoresis to evoke an axon reflex-mediated sweat response. Recording sites include the forearm, proximal leg, distal leg, and proximal foot. The TST utilizes a dedicated heat- and humidity-controlled cabinet to produce a whole-body sweat response that can be quantitated as a percentage of body surface sweating and not sweating.

The distribution of abnormal sweat responses is of diagnostic importance for a number of conditions such as peripheral neuropathy. For example, small-fiber neuropathy with the symptom of burning feet can be associated with idiopathic disease and also with diabetes. In such cases, the most distal sites may have abnormal QSART and TST responses with more proximal sites becoming involved as the disease progresses. Using a 10-point composite autonomic severity score that they developed, Drs Sandroni, Low, and Fealey found that sudomotor testing is highly sensitive in identifying clinical distal small-fiber neuropathy in patients who have normal or unrelated abnormalities on electromyographic testing. As Dr Sandroni notes, "This is a condition for which we get a lot of referrals. It is very difficult to diagnose it unless carefully controlled sudomotor testing is done."

Cardiovascular and Adrenergic Function Tests

The 2 main tests of cardiovascular function in the autonomic test sequence are heart rate response to deep breathing and the Valsalva ratio, which involves several calculations and up to 4 maneuvers.

The measure used for Valsalva ratio is beat-to-beat blood pressure. Once an invasive technique, measurement of beat-to-beat blood pressure can now be done with a recording device placed on the patient's finger. Heart rate, systolic



Robert D. Fealey, MD

Continued on page 7

Research Highlights

Mayo Clinic Study Finds the Earliest Evidence of Memory Decline in Middle-aged People at Genetic Risk for Alzheimer Disease

A Mayo Clinic–led study published in the July 16 issue of the *New England Journal of Medicine* suggests that the carriers of a common genetic risk factor for Alzheimer disease begin to have memory declines in their mid 50s, far earlier than previously thought. These and other findings support the possibility that future Alzheimer treatments may be most effective if started in middle-aged people, years before the onset of disabling memory and thinking problems or extensive brain pathology. Richard J. Caselli, MD, was the study's lead researcher.

Researchers Find Agents that Speed Up Destruction of Proteins Linked to Alzheimer Disease

A research team led by Mayo Clinic investigators has shown that druglike compounds can speed up destruction of the amyloid β ($A\beta$) proteins that form plaque in the brains of patients with Alzheimer disease. Malcolm A. Leissring, PhD, was the study's lead researcher. The study was published online in *PLoS ONE* on April 22, 2009.

Sleep Disorders Affect Majority of Elderly Participants in a Large Mayo Clinic Study

At the 2009 American Academy of Neurology annual meeting, Jennifer R. Molano, MD, and Bradley F. Boeve, MD, reported that 59% of 892 people between the ages of 70 and 89 years had signs of at least 1 recognized sleep disorder other than insomnia. The most common disorder, reported by 32% of study participants, was sleep-related leg cramps.

Anemia Might Be Associated With Development of Parkinson Disease

Results of a new study support an association between anemia experienced early in life and the development of Parkinson disease many years later. The findings were presented at the 2009 American Academy of Neurology annual meeting. Researchers included Walter A. Rocca, MD, Rodolfo Savica, MD, Justin M. Carlin, Brandon R. Grossardt, James H. Bower, MD, and Demetrius M. Maraganore, MD.

Study Finds That Surgical Treatment of Arteriovenous Fistulas Is Safe and Effective

A study by Giuseppe Lanzino, MD, found that surgical treatment of spinal arteriovenous fistulas is safe and effective. Newer techniques like endovascular embolization have not yet been demonstrated to be as effective as traditional surgery and therefore must be studied further. This study was presented at the American Association of Neurological Surgeons 2009 annual meeting.

Study Finds Posterior Fossa Exploration Surgery Provides Best Pain Relief for Trigeminal Neuralgia

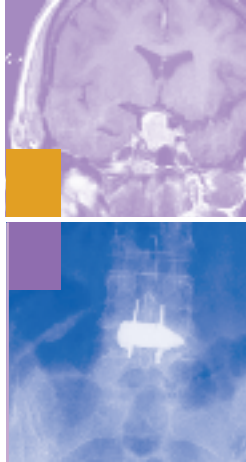
A study was presented by Bruce E. Pollock, MD, at the 2009 American Association of Neurological Surgeons annual meeting found that posterior fossa exploration surgery provided significantly better pain relief than stereotactic radiosurgery for patients with trigeminal neuralgia.

Frequency That Parkinson Disease Medication Triggers Destructive Behaviors Identified

A study published in the April 2009 issue of *Mayo Clinic Proceedings* by J. Michael Bostwick, MD, J. Eric Ahlskog, MD, PhD, and others reported that 1 in 6 patients receiving therapeutic doses of certain drugs for Parkinson disease develops new-onset, potentially destructive behaviors, notably compulsive gambling or hypersexuality.

Researchers Suspect a Novel Gene Is Causing Restless Legs Syndrome in a Large Family

In the February 2009 issue of *Mayo Clinic Proceedings* researchers reported that restless legs syndrome found in a single family is likely due to a gene mutation that has not been linked previously to the disorder. To date, 5 loci, or areas on the genome, have been linked to restless legs syndrome in other families around the world, but the family described in this article does not have any of those mutations. Authors include Carles Vilariño-Güell, PhD, Siong-Chi Lin, MD, Matthew J. Farrer, PhD, and Zbigniew K. Wszolek, MD.



To read more about Mayo Clinic neurosciences research and patient care, visit www.mayoclinic.org.

Mayo Clinic, Jacksonville, Florida, Brings Intraoperative MRI to the Region



Robert E. Wharen Jr, MD



Kurt A. Jaeckle, MD

Numerous studies have shown that total or near-total resection of brain tumors is associated with a delay or absence of tumor progression, independent of age, degree of disability, and tumor grade. Intraoperative MRI (iMRI) is an important technological step forward in achieving more complete resection, as well as in preserving critical brain structures and improving overall survival outcomes.

The newly installed iMRI at Mayo Clinic Hospital in Jacksonville, Florida, is the only unit in the surrounding geographic region. A similar unit is available at Mayo Clinic's Rochester, Minnesota, campus as well. Robert E. Wharen Jr, MD, a neurosurgeon at Mayo Clinic in Jacksonville, and his neuro-oncology colleague, Kurt A. Jaeckle, MD, note that by allowing surgeons to check their work during surgery, patient safety is increased. This technology will improve precision not only in tumor removal, but also in numerous other procedures, including epilepsy surgery. It will also provide a real-time neuronavigational tool for catheter placement and implanting deep brain stimulators. Mayo's scanner has the same image quality and tesla strength as

hospital scanners outside the surgical suite. The iMRI unit in Florida can be moved over the patient (Figure). The unit in Minnesota is in a room adjacent to the operating room, and the patient and operating table are moved between the operating room and the MRI suite.

Recent articles in peer-reviewed journals have documented the positive effect of iMRI on diverse neurosurgical outcomes in both children and adults. Because iMRI facilitates more aggressive resection with less risk of compromising healthy tissue, it has been found to improve functional outcome as well as survival rates in patients.

Impact of iMRI on Cancer Treatment Protocols

Intraoperative MRI will also impact cancer treatment at Mayo Clinic, which provides patients with access to National Cancer Institute-funded clinical trials through the North Central Cancer Treatment Group (NCCTG) and the 3-site Mayo Clinic Cancer Center. As Dr Wharen points out, "Many of the available treatments in ongoing clinical trials are more effective with prior surgical

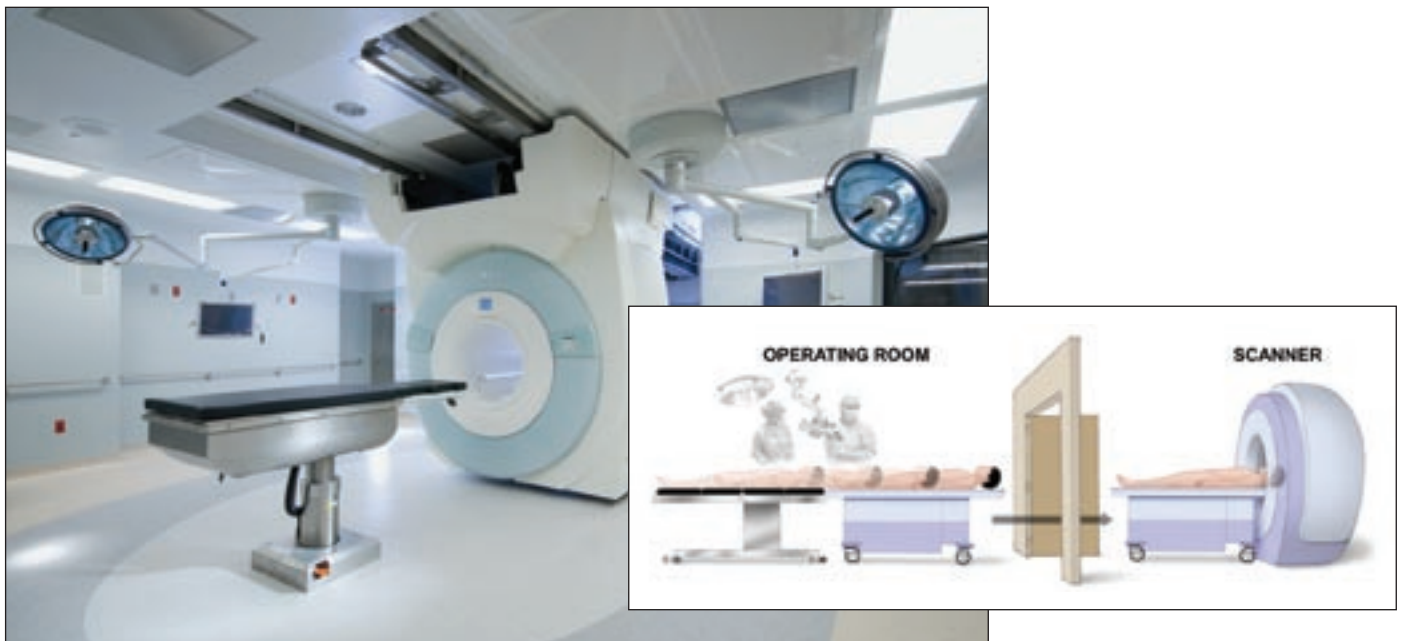


Figure 1. The iMRI unit in Florida can be moved over the patient (left). The unit in Minnesota is in a room adjacent to the operating room, and the patient and operating table are moved between the operating room and the MRI suite (right).

removal of the tumor. The more complete the removal, the better the chance that adjunct therapies will work.”

In addition to its clinical impact, iMRI will play an important role in Mayo’s cancer treatment research. Dr Jaeckle points out that

iMRI will assist surgeons in more precisely obtaining targeted tissue during the surgical procedure so that scientists can then determine whether the chemotherapeutic agent reached the site and had the predicted effects.

The Utility of Autonomic Testing *Continued from page 4*

blood pressure, and diastolic blood pressure are continuously displayed on a computer screen. The Valsalva maneuver is measured during 4 main physiologic phases. Drs Low and Sandroni and their colleagues have validated the use of the phases in evaluating adrenergic function.

Beat-to-beat blood pressure under various laboratory conditions is a proven method of testing adrenergic function for many conditions, including orthostatic hypotension (OH) (Figure on page 3). OH is well recognized as a potential consequence of PD and diabetes and is increasingly recognized as a common disorder among the elderly. Symptoms of OH such as fatigue and impaired concentration can be subtle and difficult to diagnose. Even when mild, symptoms of OH can be debilitating and markedly affect activities of daily living. Severe and sustained OH can induce syncope with resultant falls and injury. In younger patients, symptoms may

include palpitations, anxiety, and nausea and may be indicative of autonomic neuropathy. Adrenergic testing helps distinguish OH syncope from psychogenic disorders and from other conditions that induce loss of consciousness such as seizures and transient ischemic attacks. Autonomic tests can also determine severity of OH, an important factor when considering behavioral, pharmacologic, and nonpharmacologic treatments.

In discussing the value of Mayo’s autonomic testing laboratory, Dr Low notes that “it highlights the complexity of the autonomic system.” He goes on to say, “Although we can’t dissect all aspects of autonomic function, what we can do is detect deficits that may have gone undiagnosed, determine if the problems are benign or represent a true autonomic failure, and, if so, quantify its severity and distribution.”

Recognition

Mayo Clinic physicians were honored to receive the following awards from their colleagues at meetings of the American Academy of Neurology, the American Association of Neurological Surgeons, and the Society of Neurological Surgeons.

A. B. Baker 2009 Teacher Recognition Award

Allen J. Aksamit Jr, MD

A. B. Baker 2009 Award for Lifetime Achievement in Neurologic Education

Jasper R. Daube, MD

Distinguished Service Award

David G. Piepgras, MD

Jon Stolk 2009 Award in Movement Disorders for Young Investigators

Christian W. Wider, MD, Research Fellow

Recipient of an AAN Clinical Research Training Fellowship

Daniel O. Claassen, MD

Stryker Award for Neuro-oncology

Andrew B. Foy, MD

Cloward Fellowship Award

Marie-Noëlle Hébert-Blouin, MD

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CME Opportunities

Mayo Clinic Stroke and Cerebrovascular Disease Review

September 11-13, 2009, Amelia Island, Florida

This course will provide attendees with an update across all major areas of clinical interest in stroke and vascular neurology. Lectures will cover the latest in management of acute ischemic stroke and brain hemorrhage, as well as asymptomatic vascular lesions, including arteriovenous malformations, cavernous malformations, cerebral aneurysms, and carotid stenosis. The course will also cover the latest diagnostic and therapeutic approaches to brain attack. The major single-gene disorders that cause stroke will be reviewed. Lectures will be supplemented with highlights of images in clinical vascular neurology.

Contact: 800-462-9633 or cme@mayo.edu

Neuroradiology: Practice to Innovation

November 2-6, 2009, Scottsdale, Arizona

This course is designed for the practicing radiologist whose work involves neuro-radiology or those involved in the neurologic sciences, neurosurgery, neurology, and related fields. It is intended to provide an update in new trends, relevant techniques, and applications in diagnostic and therapeutic neuroradiology.

Contact: 866-246-1581 or cme@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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