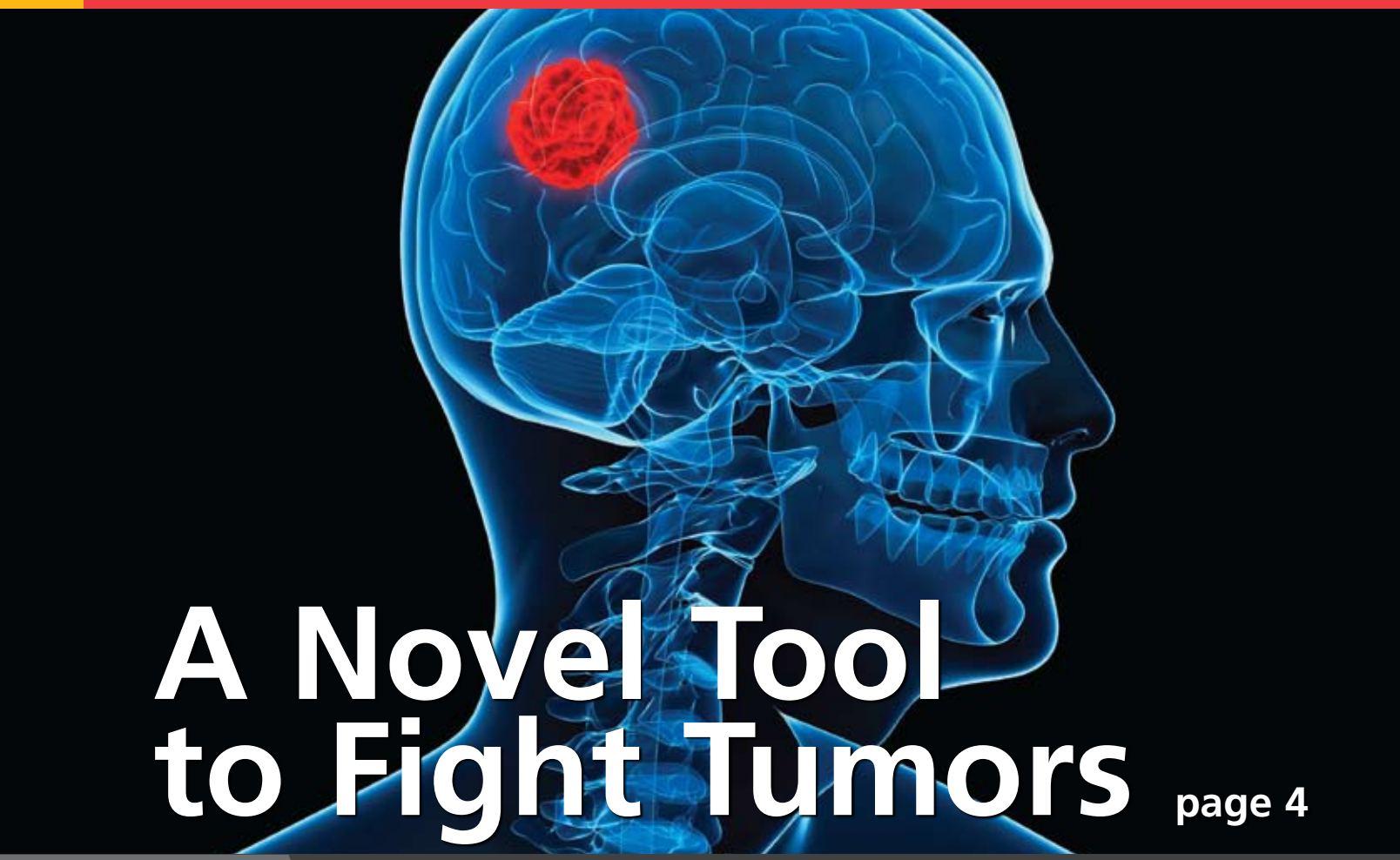
University Hospitals
Case Medical Center

Cleveland | Ohio

UH Innovations In Neurosciences

University Hospitals Neurological Institute



A Novel Tool to Fight Tumors

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Always Advancing

The University Hospitals Neurological Institute is committed to developing innovative, integrated and individualized care for patients with neurological conditions. This spirit of innovation drives our efforts to provide high value health care by improving our patients' long-term outcomes.

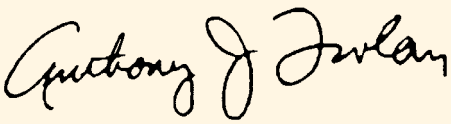
Two of our newest Centers of Excellence create an infrastructure to apply the principles of evidence-based practice across the full continuum of patient care, from initial diagnosis through follow-up visits. The Neuroscience Nursing Practice Center bridges the gap between nursing research and clinical practice by giving nurses the tools to evaluate and apply new findings in a caring, patient-centered environment. The Neurological Outcomes Center teams clinicians with experts in outcomes sciences to evaluate and define performance improvement measures that enhance quality, improve outcomes and provide high value health care. Both centers are among the first of their kind in the nation.

This issue of *UH Innovations in Neurosciences* highlights some of these ongoing efforts within the Neurological Institute. Unique interdisciplinary clinics for autonomic disorders at the UH Neurological Institute are attracting referrals of patients from across the United States. Our neurosurgeons are testing a promising new minimally invasive procedure for glioblastoma multiforme that combines laser energy with real-time MRI guidance. At our Memory and Cognition Center, neurologists are analyzing data from a National Institute on Aging study to find ways to identify people with mild cognitive impairment who will progress to dementia. The neurointerventional team is helping to define best practices in treating cerebral aneurysms by comparing endovascular placement of a coil with microsurgical clipping.

We welcome your inquiries about the UH Neurological Institute, and hope you will entrust us to provide your patients with innovative and compassionate care.

Sincerely,

Warren R. Selman, MD
Director, UH Neurological Institute
University Hospitals Case Medical Center
The Harvey Huntington Brown Jr. Professor and Chair,
Department of Neurological Surgery
Case Western Reserve University School of Medicine



Anthony J. Furlan, MD
Co-Director, UH Neurological Institute
University Hospitals Case Medical Center
Gilbert W. Humphrey Professor and Chair,
Department of Neurology
Case Western Reserve University School of Medicine

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Contributors: Warren R. Selman, MD; Anthony J. Furlan, MD;
Thomas C. Chelimsky, MD; Alan J. Lerner, MD; Andrew Sloan, MD; Robert W. Tarr, MD
Publication Coordinator: Brea Weisman

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Among the nation's leading academic medical centers, University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a nationally recognized leader in medical research and education.

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

The commitment to exceptional patient care begins with revolutionary discovery. Faculty at the Case Western Reserve University School of Medicine, who also are physicians at UH Case Medical Center, are at the forefront of medical research and innovation. The School of Medicine is the largest medical research institution in Ohio and among the nation's top medical schools for research funding from the National Institutes of Health.

Unraveling Medical Mysteries

Interdisciplinary clinics focus on autonomic disorders

Thomas C. Chelimsky, MD, Director, Autonomic Laboratory, UH Neurological Institute, University Hospitals Case Medical Center, is chair-elect of the American Academy of Neurology Pain Section and serves on the board of directors of the American Autonomic Society.

Thomas C. Chelimsky, MD, likes to tackle the complex cases that have baffled primary care physicians and specialists – cases in which a patient suffers from a plethora of symptoms that resist conventional treatment. Probing the relationships among those symptoms and helping patients achieve a normal life is his mission, and that of the teams of specialists who staff four interdisciplinary clinics for autonomic disorders at the University Hospitals Neurological Institute.

Dr. Chelimsky is Director, Autonomic Laboratory, UH Neurological Institute, University Hospitals Case Medical Center, and Professor, Neurology, Anesthesiology and Pediatrics, Case Western Reserve University School of Medicine. He and his wife, Gisela Chelimsky, MD, a pediatric gastroenterologist, pioneered a new approach to autonomic disorders when they established the Pediatric Autonomic Interdisciplinary Clinic in 2006. To complement their own areas of expertise, they recruited specialists in pediatric psychology, cardiology and sleep disorders. Today the UH Neurological Institute has the only complete autonomic laboratory in Ohio and the only one in the United States that assesses children.

Seeking Complex Cases

"We focus on kids with abdominal complaints and other symptoms such as headaches or fainting," says Dr. Chelimsky. "Often a child's pediatrician doesn't initially see an association between one symptom and another, so they may be unsuccessfully treating them as separate disorders. Putting the different symptoms together can lead pediatricians to suspect a problem with the autonomic nervous system, the control center for the bowel, bladder and blood pressure. At that point, the child may be referred to our clinic. We rarely see anyone who hasn't been evaluated by one or two doctors already."

Additional autonomic disorder clinics and their specialists include:

- **Chronic pelvic pain:** anesthesia, psychology, urology, gynecology, neurology
- **Complex regional pain syndrome:** anesthesia, psychology, neurology
- **Dizziness and fainting:** cardiology, psychology, neurology, endocrinology
- **Sweat disorders (planned for 2010):** neurology, neurosurgery, dermatology, anesthesia

Empowering the Patient

"The psychologists play a key role in the evaluation of all our patients," says Dr. Chelimsky. "They can figure out if the patient is depressed, and if so, whether the depression preceded the symptoms or came later. They also help with the tremendous anxiety that can exacerbate patient symptoms." For example, Dr. Chelimsky explains, fear of fainting causes anxiety, and anxiety can cause fainting by triggering a "sympathetic storm" in which heart rate and blood pressure increase, then drop. "Our goal is to put the patient in control," he says, "to empower the patient to live a normal life without the symptoms of their disease. So just teaching the patient a substitute exercise that will cause them to relax could avert the increase in pain, or the fainting."

Physicians associated with the clinic maintain electronic medical records (EMRs) to track patient data, teaching schedules and study enrollment. The group is also developing Web-based patient questionnaires that will be integrated with the EMRs to enhance the efficiency and effectiveness of patient visits and allow long-term follow-up.

News of the interdisciplinary clinics has spread quickly, thanks to patient support groups on the Internet, and Dr. Chelimsky says he sees patients from across the country. He has received a grant from the National Institutes of Health for a five-year study to investigate the relationship of stress to interstitial cystitis, an autonomic disorder affecting the bladder. Another grant from the Earl and Doris Bakken Foundation is directed toward complex regional pain syndrome research.

Conversations among specialists have been a driving force in his effort all along, says Dr. Chelimsky. "Nothing is more exhilarating in medicine than to feel like you're hitting new frontiers. When you're stuck in thoughts you've had for years, it's hard to move on, but when you have someone else to bounce things off of, and they've been trained differently than you have, you start seeing things that you never saw before."

Expert Advice

If you need some direction about a specific patient, e-mail a three-sentence summary of the case to Thomas Chelimsky, MD, at **Thomas.Chelimsky@UHhospitals.org**.

Exploring a New Treatment Modality

UH tests a novel procedure combining lasers and MRI against malignant brain tumors

Andrew Sloan, MD, is a co-principal investigator for the Adult Brain Tumor Consortium at the Case Comprehensive Cancer Center. He has received numerous grants from the National Institutes of Health for his glioma research.

The death of Sen. Edward M. Kennedy, who had been diagnosed with a glioblastoma multiforme (GBM), drew national attention to the challenges of treating these and other malignant brain tumors. According to the National Brain Tumor Society, a GBM is the most invasive type of glial tumor and accounts for 23 percent of all primary brain tumors. A GBM is diagnosed in about five of every 100,000 Americans each year. Few significant treatment advances have been achieved in the past 25 years; median survival with treatment is approximately 12 months.

MRI-Guided Laser Therapy

In an effort to halt tumor growth and extend the survival of patients with GBM, University Hospitals Neurological Institute surgeons are investigating a new, minimally invasive procedure that combines laser interstitial thermal therapy (LITT) with real-time magnetic resonance imaging (MRI) guidance. The procedure utilizes the AutoLITT™ System, new technology developed by a Canadian medical device firm. The system was tested in humans for the first time in a Phase I clinical trial at the National Institutes of Health-designated Case Comprehensive Cancer Center at Case Western Reserve University School of Medicine. Principal investigator for the trial at UH is **Andrew Sloan, MD**, Director, UH Neurological Institute Brain Tumor and Neuro-Oncology Center; holder of the Peter D. Cristal Chair in Neurosurgery; and Associate Professor, Neurological Surgery, Case Western Reserve University School of Medicine.

"Neurosurgeons have been operating with lasers for 30 years," Dr. Sloan points out. "What makes this procedure different is that instead of using a simple 'recipe' for how to fire the laser and using it as part of a conventional open surgical procedure, we're using a minimally invasive approach, operating through a burr hole and using the MRI as our 'eyes.' Guiding treatment based on a genetic formula, we tailor the treatment precisely to the tumor using real-time MRI."

The system uses a standard 1.5 Tesla MRI scanner and an MRI-compatible laser probe. Unlike conventional surgery, which requires a craniotomy, the surgeon makes a small incision and burr hole, then inserts a fiber-optic catheter through the burr hole directly to the tumor site under the direct visual guidance of the MRI. The laser is activated through the fiber-optic catheter to heat and coagulate the tumor from the inside. This allows the surgeon to carefully dissect away the tumor from the inside out, even deep within delicate regions of the brain, with little or no damage. The heat is generated in one direction only; in all other directions, the probe cools to protect healthy tissue surrounding the tumor. MRI thermometry measures temperature in and around the tumor and provides the surgeon with real-time feedback, while positioning and monitoring devices allow the surgeon to control the procedure without moving the patient in the MRI.

Treatment Results

Dr. Sloan and colleagues tested the AutoLITT System in 2008 and 2009 on 10 adult patients with GBM. All had tumors that had recurred after treatment with surgery or radiation and chemotherapy. "The median survival in this group of patients [with recurrent GBM] is about four months," he says. "A number of considerations, including the shape and location of the tumor, can make these tumors very difficult to treat. With the AutoLITT System, our ability to precisely contour the treatment to the tumor through a minimally invasive approach using real-time MRI is superior to what we can achieve using conventional techniques. This enables us to perform maximal resection with minimal damage, even within critical and delicate locations."

Results of the trial, which was intended to determine the safety of the new treatment, established that it was safe even at the highest dose administered. "The side effects of the procedure were minimal," Dr. Sloan says. "There was some swelling and edema, but far less than we expected." Imaging studies performed on patients following the procedure indicated that tumor growth had been halted, at least temporarily, and the tumors had lost their enhancement. The AutoLITT System received U.S. Food and Drug Administration clearance in May 2009 for use in neurosurgery. Dr. Sloan presented his findings at the 2009 joint meeting of the Society of Neuro-Oncology and the American Association of Neurological Surgeons/ Congress of Neurological Surgeons Section on Tumors.

Top: Patient being treated in MRI. Bottom, from left: Thin (3mm) side-firing laser probe enables neurosurgeon to precisely sculpt treatment to the entire tumor; Monteris catheter targeting the tumor; zoom of laser entering and destroying the tumor.

Although the trial was not designed to evaluate the efficacy of the treatment, Dr. Sloan says he is encouraged enough by the patients' response to continue to use the AutoLITT System.

Future Research

If the treatment is proved effective against recurrent GBM, it likely will be tested more broadly, according to Dr. Sloan. "Should we use it only for gliomas? Can it be used for benign tumors as well? Should it be used upfront for gliomas or only in recurrent settings? These are questions that we have not yet answered but will be the goal of the next major research." Longer term, the manufacturer's mission statement declares the company's intention to explore the application of AutoLITT technology to the treatment of pediatric brain tumors.

Note: The AutoLITT System is manufactured by Monteris Medical of Winnipeg, Manitoba. Dr. Sloan is an investigator and a paid consultant to Monteris.

Learn More

For additional information about neurosurgical options using the AutoLITT System, call Jennifer Jochum at **216-844-6054**.

New Directions in AD Research

Alzheimer's disease experts at UH study patients with mild cognitive impairment

Alan J. Lerner, MD, has served as site principal investigator for more than 30 clinical trials and is the editor of four neurology textbooks.

Alzheimer's disease (AD), the most common form of dementia, threatens a growing segment of the United States population, those age 65 and older. According to National Institutes of Health (NIH) estimates, the number of elderly Americans is expected to increase from 39 million in 2008 to 72 million in 2030, and the number of people with AD doubles for every five-year interval beyond age 65. The Alzheimer's Association estimates that as many as 5.3 million people are currently living with AD; by 2050, one American will develop the disease every 33 seconds. With no prospect of a cure in the near term, University Hospitals Neurological Institute physicians at University Hospitals Case Medical Center are battling AD on multiple fronts.

Early Diagnosis

"We're participating in a major NIH study that's looking at elderly people with mild cognitive impairment [MCI] – those who are on the cusp of dementia, who are starting to show symptoms but haven't met all the diagnostic criteria of dementia," says **Alan J. Lerner, MD**, Director, UH Neurological Institute Memory and Cognition Center, and Professor, Neurology, Case Western Reserve University School of Medicine. "This is a group of tremendous interest, because if and when we do get effective treatment, the first thing we have to do is recognize the condition early."

The AD Neuroimaging Initiative (ADNI), a five-year study conducted by the National Institute on Aging (a component of NIH), was launched in 2004 to examine normal cognitive aging, MCI and AD. A key goal is to facilitate the development of neuroimaging technologies used in AD research and diagnosis, including magnetic resonance imaging (MRI) and positron emission tomography (PET). Investigators are collecting serial clinical, neuropsychological, biological and imaging data on 400 elderly people with MCI, 200 with early AD and 200 with normal cognition.

Dr. Lerner is analyzing data from ADNI participants with Curtis Tatsuoka, PhD, Associate Professor of Neurology, Case Western Reserve University School of Medicine. "We've chosen to look at neuropsychological and genetic data of people with confirmed AD and with MCI. We're using a sophisticated statistical technique to try to identify those people with MCI who will progress to more severe cognitive impairment and dementia," says Dr. Lerner. "It would be of great value to primary care physicians if we can say, ultimately, these are the neuropsychological profiles of the people you want to identify and treat early. Because ADNI is a longitudinal study, we know that as many as 35 percent of those

people in the initial cohort of 400 with MCI have already converted to AD. Additionally, a new cohort study entitled ADNI GO received funds from the American Recovery and Reinvestment Act of 2009 and will be looking at cognitive trajectories in more mildly affected individuals with early MCI."

Imaging and Next-Generation Treatments

Researchers at the Memory and Cognition Center are investigating several new compounds for in vivo PET imaging of amyloid deposition in the brain, Dr. Lerner says. "I see this as the wave of the future," he adds. "Many of our studies now have a PET substudy. We're looking at a number of different compounds that bind directly to brain amyloid."

Dr. Lerner's group is also testing several new treatments for AD. University Hospitals is a site for the Phase III Gammaglobulin Alzheimer's Partnership Study, which will examine the safety, effectiveness and tolerability of gammaglobulin in patients with mild to moderate AD. "This is a treatment aimed directly at amyloid; gammaglobulin may bind to and interfere with amyloid metabolism and deposition in the brain," says Dr. Lerner. "This is a very exciting time, because as America grays, these issues are going to become bigger, not smaller. I think there's significant progress in understanding AD; treatment is a different question. There's a lifetime's worth of work ahead."

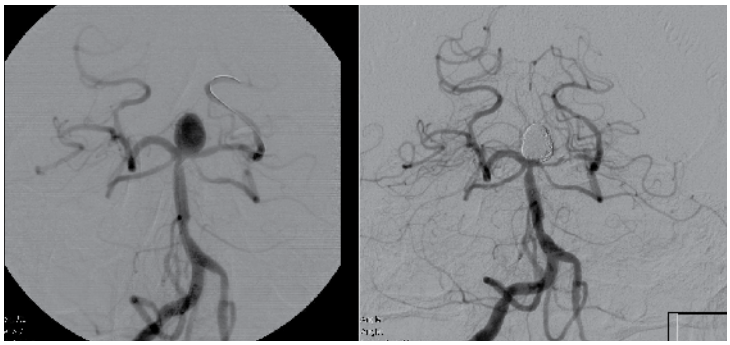
Enroll Your Patients

To inquire about ongoing clinical trials and patient referrals, call the Memory and Cognition Center at **216-464-6412** or visit **UHhospitals.org/neuro/clinicaltrials**.

The Endovascular Alternative

UH physicians weigh clip versus coil for cerebral aneurysms

For a patient with two cerebral aneurysms, the treatment administered by the neurointerventional team at University Hospitals Case Medical Center demonstrated the dramatic advances achieved in non-invasive endovascular neurosurgery. The same case also illustrated the advantage of having neurosurgeons on staff with expertise in microsurgical techniques for cerebrovascular disorders who can safely perform a craniotomy for microsurgical clipping, the more traditional treatment for cerebral aneurysms.



Two Aneurysms, Two Approaches

The patient, a 62-year-old man, presented with unruptured cerebral aneurysms in two different locations. "One was at the basilar tip, where the risk to the patient is much higher with open surgery than with an endovascular procedure," says **Robert W. Tarr, MD**, Section Chief, Neuroradiology, UH Case Medical Center, and Professor, Radiology, Neurology and Neurosurgery, Case Western Reserve University School of Medicine. "The other aneurysm had a different kind of anatomy – normal arteries arose from the base of the aneurysm. Generally we find that an open surgical procedure is more effective for an aneurysm with this structure because it can be difficult to keep the normal arteries open with an endovascular technique."

After evaluating the patient and discussing the treatment options, the multidisciplinary team of neurointerventional radiologists and neurosurgeons recommended endovascular placement of a coil and stent to treat the basilar tip aneurysm and open surgery for the wide-necked aneurysm. The endovascular procedure was performed first, followed by the open surgical procedure two and a half months later. "The patient had some visual impairments after the endovascular procedure, but those resolved and he has done well since, with no evidence of recurrence," says Dr. Tarr.

Minimally Invasive Procedure Proving Effective

A study published in *The Lancet* (2005;366:809-17) compared the clinical outcomes associated with endovascular coiling versus neurosurgical clipping in the treatment of ruptured subarachnoid aneurysms. The International Subarachnoid Aneurysm Trial has "changed the practice of treating aneurysms," says Dr. Tarr. Results of the multicenter, randomized, controlled trial showed that in patients with a ruptured aneurysm suitable for either treatment, endovascular coiling is more likely to result in independent survival at one year than microsurgical clipping, and the survival benefit continues for at least seven years.

Since the first platinum coils were approved by the FDA in the mid-1990s, several technological advances have contributed to their increasing role in the treatment of cerebral aneurysms, Dr. Tarr explains. Newer designs are more flexible, with a three-dimensional shape that can fill complex aneurysms. Some have bioactive properties that cause them to swell and prevent blood from flowing into the aneurysm. In the case described, a thin-walled stent was placed in the normal part of the artery to bridge the neck of the aneurysm and help hold the coil in place.

Robert W. Tarr, MD, is immediate past president of the Society of NeuroInterventional Surgery and site principal investigator for the Stenting vs. Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial, funded by the National Institutes of Health.

Selecting the Optimal Treatment

The UH team considers several factors when deciding how to treat a patient with a cerebral aneurysm. In patients with an *unruptured* aneurysm, there is no data suggesting one form of treatment is superior to the other, and it is important to have a cerebrovascular team that is equally facile and safe with both. "Patients who come to us with ruptured aneurysms may already have swelling in the brain. If they do, it's safer to use endovascular," says Dr. Tarr. "We also consider confounding medical issues, such as cardiac or respiratory. But if an artery is branching off from the wall of an aneurysm, you need to consider microsurgery because the aneurysm clip can be adjusted to preserve the normal branch."

Although he admits to a slight bias in favor of endovascular procedures, Dr. Tarr says he is glad to have two experienced vascular neurosurgeons on the team. "Endovascular is certainly a growing alternative to treat aneurysms, but I don't think it's the best treatment for every aneurysm, or for every patient. Fortunately, at University Hospitals Case Medical Center, we can offer our patients both options."

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To request a copy or view online, visit **UHhospitals.org/NIJournal**.

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University Hospitals Neurological Institute

University Hospitals Neurological Institute at Case Medical Center in Cleveland, Ohio, is the area's first designated neurological institute providing integrated and comprehensive care for patients with diseases affecting the nervous system.

Our 15 Centers of Excellence offer you premier care and access to some of the country's foremost experts in neurology, neurosurgery, neuroradiology, neuro-oncology, neuro-ophthalmology, neurotology, neuropathology, neuropsychology and related specialists. These teams work in collaboration with medical specialists at Rainbow Babies & Children's Hospital and the Ireland Cancer Center, with access to the UH Neuroscience Intensive Care Unit and NeuroScience Nursing Practice.

A relationship with UH doctors provides you:
- **Access:** 48-hour referral access for urgent cases.
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- **Professionalism:** Our goal is to return referred patients to you for ongoing care.
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Whether referring patients to University Hospitals for a second opinion or treatment of complex diseases, the integration between physician specialists and researchers allows for the development of an individualized treatment plan based on patient-centered needs.

Sending your patients to the University Hospitals Neurological Institute provides:
- **State-of-the-Art Care:** Access to the Neuroscience Intensive Care Unit.
- **Personalized Treatment Plans:** Developed by a multidisciplinary team of physicians.
- **Caring Environment:** Availability of the Neuroscience Nursing Practice.
- **Cutting-Edge Advancements:** Access to research results and the latest clinical trials.

Physicians in the University Hospitals Neurological Institute are here to partner with you to provide fully integrated, personalized care to your patients. For immediate decision-making advice from UH neurological or neurosurgical experts, call **216-844-1001**.

For more information on the Neurological Institute or to transfer a patient, please call 1-866-UH4-CARE (1-866-844-2273) or visit us on the Web at UHhospitals.org/neuro.

To receive decision-making advice from UH neurological or neurosurgical experts, call 216-844-1001.