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Collaborative Management of Pediatric Brain Tumor at Mayo Clinic

It may take longer to recognize the symptoms of brain tumor in infants and children than it does in adults. At Mayo Clinic in Rochester, Minnesota, once a tumor is suspected, efficient integration across pediatric oncology, neurology, neuro-radiology, neurosurgery, and neuropathology smoothes the diagnostic process. Collaborating in every aspect of pediatric care at Mayo Clinic's T. Denny Sanford Pediatric Center and the Eugenio Litta Children's Hospital, the medical team can typically arrive at a diagnosis over the course of several days rather than weeks.

Symptoms: Specific and Nonspecific

Children with brain tumors may have obvious neurologic signs such as focal sensorimotor deficits or asymmetric motor skills indicative of a tumor. Other readily recognized signs include hydrocephalus, balance and coordination problems (Figure 1), seizures (Figure 2, see page 2), failure to reach

developmental milestones, or the loss of those previously gained.

Often, however, the symptoms are less specific. For example, persistent vomiting over the course of 2 to 3 weeks without other gastrointestinal tract or respiratory tract signs or fever might be a response to pressure within the brain from a tumor. Other nonspecific symptoms include persistent headache (Figure 3, see page 2), lethargy, failure to gain weight, and frequent thirst, drinking, and urination. In older children, the signs may include head tilt and eye deviation.

Collaborative Diagnosis

All initial work-ups for new brain tumor patients are managed by a designated pediatric neurologist who coordinates consults with any of Mayo's 9 other pediatric neurologists, a pediatric oncologist and often with a radiation oncologist and pediatric neurosurgeon. Anesthesiologists with special expertise in pediatrics sedate children for imaging studies, paying particular attention to each patient's age and severity of illness. Tests for brain tumors in children at Mayo may include CT scan, MRI, MR spectroscopy, and, in some cases, PET scans.

If seizures are present, pediatric epilepsy specialists help determine if the tumor alone is causing the seizures. Mayo Clinic has extensive experience in 24-hour video monitoring for epilepsy before surgery. Pediatric neuropsychologists provide behavioral and developmental testing. Specialists in pediatric endocrinology and genetics are also available as needed.

Surgical and Medical Management

Surgical resection is considered the best treatment for most childhood brain tumors. Because chemotherapy and radiation therapy pose risks for the developing brain, removing as much of the tumor as possible is critical. Nicholas M. Wetjen, MD, a pediatric neurosurgeon, notes, "Too often we see patients in whom the tumor has been incompletely



Figure 1. Medulloblastoma in a 4-year-old boy who presented with nausea, vomiting, and imbalance. MRI demonstrated a large, hypointense tumor in the midline cerebellum with associated obstructive hydrocephalus.



Nicholas M. Wetjen, MD

resected or an inadequate tissue sample has been collected for biopsy. Then we are dealing with both the adverse effects of surgery and the need to redo the surgery.”

At Mayo, an initial biopsy for pathology testing can often be conducted during the surgical procedure. Cynthia J. Wetmore, MD, PhD, a pediatric neuro-oncologist, points out, “Even if the tumor is completely resectable, adjunct chemotherapy or radiation therapy often improves long-term survival, except in children less than 3 years old, for whom radiation is not recommended.”

Among the many research initiatives in the pediatric neuro-oncology program at Mayo, radiation oncologist Nadia N. Laack, MD, and colleagues are investigating the long-term effects of radiation therapy on cognitive development and growth. Dr Wetmore is investigating pediatric tumor resistance to radiation therapy and ways to target tumors without harming normal brain development. Pediatric neurologist Gesina F. Keating, MD, and colleagues are studying long-term outcomes following pediatric brain tumor diagnosis and treatment.

Mayo offers state-of-the-art neurosurgical techniques, including the ability to conduct electrophysiologic and speech and language monitoring during surgery, frameless stereotactic surgery for real-time intraoperative localization and navigation, and intraoperative MRI. Mayo



Cynthia J. Wetmore, MD, PhD



Gesina F. Keating, MD

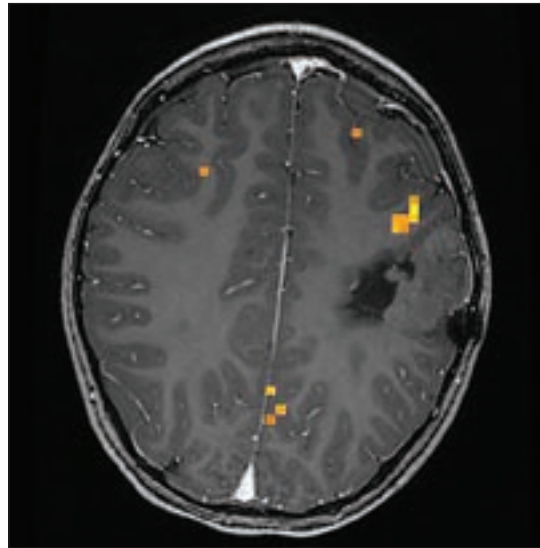


Figure 2. An 8-year-old girl presented with right-sided weakness and intractable epilepsy since the age of 2 years. The tumor was thought to be unresectable due to its location and proximity to the motor cortex. Functional MRI scan during opening and closing of the hand demonstrates that the motor cortex (yellow dots represent increased blood flow) is anterior to the tumor. She underwent surgical removal of the ganglioglioma and is now seizure free, with improvement in hand function.

neurosurgeons have extensive experience in tumor resection in both the adult and pediatric practice. Experience matters. A recent study found that it is a major factor affecting pediatric brain tumor surgical outcomes.

Unlike adults, 95% of children who have chemotherapy in the United States are treated through protocols specified by the National Cancer Institute (NCI). Most clinicians involved in the direct management of pediatric brain tumors at Mayo Clinic in Minnesota are members of the Children’s Oncology Group (COG) through the NCI. All postsurgical therapy is directed by a member of COG.

Taking Care of Pediatric Patients and Their Families

Mayo Clinic’s T. Denny Sanford Pediatric Center serves more than 45,000 children a year. From its nature-inspired theme to its specialized furniture, restrooms, and drinking fountains, it is designed for children of all ages. It is a colorful, welcoming environment, but more importantly, it is staffed by pediatric experts from every specialty working together in a central location to coordinate care to the patient’s best advantage.

Mayo Clinic’s Eugenio Litta Children’s Hospital is staffed by more than 150 physicians. Distinct from, but located within Mayo’s Saint Marys Hospital, patients have access to the expertise of Mayo’s entire staff of physicians. The facility includes playrooms for all ages and a teen lounge. Tutors are available from the Rochester Public School system for children absent from school for long periods of time. Physical therapists, speech-language pathologists, and

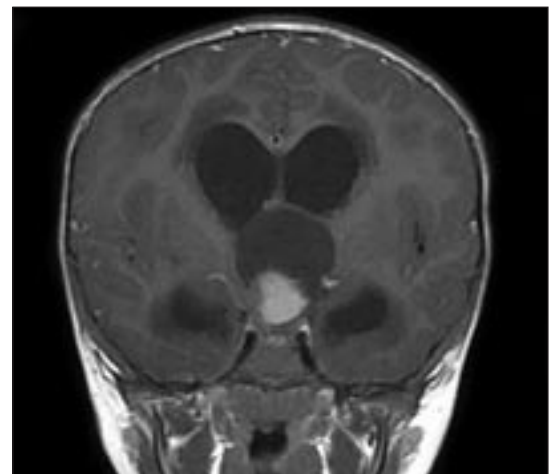


Figure 3. A 2-year-old boy with a 4-week history of nausea and a 1-week history of headache. MRI demonstrates contrast-enhancing hypothalamic tumor with an associated cyst and hydrocephalus. The patient underwent surgical removal of the tumor, and the pathology was anaplastic astrocytoma.

other pediatric rehabilitation specialists work with patients during recovery.

A diagnosis of brain tumor affects the entire family. Social workers and child-life specialists support children and families before, during, and after surgery. The hospital has special family space with laundry, kitchen, and shower facilities. Pets are permitted to visit. For patients who come from a distance, there is the Ronald McDonald House, located only blocks from the clinic and hospital. Supported by charitable

contributions and available with a Mayo Clinic referral, it has 45 rooms at a minimum cost, accommodating up to 5 persons per room, for as long as needed, be it 6 days or 6 months.

As Dr Wetmore notes, “We have a commitment to our pediatric brain tumor patients and their families that extends from our breadth and depth of interdisciplinary expertise to our brain tumor research and our child-centered, state-of-the-art facilities.”

Novel Therapies for Glioblastoma

Patients with malignant glioma, the most common and most aggressive form of primary brain tumor, have an average survival time of 12 to 16 months. With a high rate of recurrence, these tumors are resistant to conventional therapy, including surgery, radiation therapy, and chemotherapy. For all these reasons, glioblastoma is one of the key focus areas for Mayo Clinic’s brain cancer research (see *Neurosciences Update* volume 5, number 4).

Making Bench to Bedside a Reality

“A key focus of our effort is to translate promising laboratory findings into clinical trials, then, building on the clinical data, go back to the lab to create something we think is even better,” says Evanthia Galanis, MD, an oncologist with a special interest in neuro-oncology, especially glioblastoma research.

She and her colleagues are conducting pioneering work on the use of oncolytic viruses and novel targeted drug combinations. Her words highlight the interplay between the laboratory and clinical outcomes that exemplifies “bench to bedside” or “translational research.” These familiar terms represent an ideal in which laboratory and clinical findings create a continuous loop of innovations and clinical applications to improve patient care. This goal, however, can be difficult to attain, particularly within a single institution.

It requires integrated teams of researchers and clinicians and an infrastructure that provide the necessary equipment and support data analysis and clinical trials.

Sum Greater Than the Parts

Mayo Clinic is fortunate

that its own extensive infrastructure is supported by several major programs that further increase efficiency. Mayo is 1 of 4 institutions in the country to have a National Cancer Institute (NCI)-funded brain cancer Specialized Program of Research Excellence (SPORE). It also holds 4 other SPORE grants and participates in 2 more. These, in turn, are supported by Mayo’s NIH-funded Center for Translational Science Activities (CTSA) and Mayo’s 3-site, NCI-funded Cancer Center, one of the largest in the country. Finally, Mayo’s leadership in the North Central Cancer Treatment Group (NCCTG), a cooperative clinical research group for development, execution, and review of high-priority NCI-funded trials, helps expedite novel treatments into trials.

Economy of Scale

“The theme in our brain cancer SPORE is pathogenesis-based prevention and treatment of gliomas, which involves understanding the mechanisms and identifying predictors,” says Brian Patrick O’Neill, MD, the Mayo neurologist who heads the brain cancer SPORE. The SPORE is divided into 4 cores that support each phase from new initiatives to refining previous discoveries. “When Dr Galanis’s team wants specimens analyzed to understand the effects of a drug,” Dr O’Neill notes, “the clinical core provides the clinical background on each patient. The pathology core provides the diagnostic and pathology analysis, and the statistics core provides the data analysis. Thus, we have an economy of scale, driven and supported by a single institution.”

The research by Dr Galanis and her colleagues, highlighted in the following sections, exemplifies translational research in action.

Treating Tumors With the Measles Virus

Case reports in the 1970s suggested that natural infection with the measles virus (MV)



Evanthia Galanis, MD, and Brian Patrick O’Neill, MD

led to spontaneous regression of hematologic malignancies in African children. Since then, the biogenetic mechanisms of the MV have been identified and have helped clarify its potential as an oncolytic agent. Building on this information, Dr Galanis and colleagues discovered that a vaccine strain of MV causes glioma cells to fuse, thus triggering apoptosis or cell death (Figure). This agent is now in a clinical trial to assess its safety in treating glioblastoma.

During their investigation, the research team overcame a major challenge in using viral approaches to brain tumors—the limited ability to monitor the effect of the virus on a tumor in vivo, by engineering the virus to express the soluble marker carcinoembryonic antigen. To better understand the virus’s action in a nonartificial environment before human testing, Dr Galanis’s team, in collaboration with Jann N. Sarkaria, MD, a radiation oncologist and head of the brain SPORE’s animal core facility, implanted tumors extracted from patients directly into a series of animal models. In these models both the tumor and the virus performed as they do in humans. The effects were found to be positive and nontoxic.

The in vivo work dramatically expedited bringing the virus into human trials. Preliminary results suggest that it may inhibit tumor recurrence and, when used in combination with other targeted drugs, it may increase the oncolytic effects of both.

Novel Targeted Drug Combinations

Bevacizumab is an example of a “smart” or targeted drug—a drug that exploits tumor-specific molecular changes. Glioblastomas tend to be very vascular and heavily dependent on blood supply to grow. Bevacizumab works by binding to vascular endothelium growth factor (VEGF) and preventing it from signaling. VEGF is known to

increase tumor blood supply, but, as Dr Galanis points out, “while bevacizumab can lead to durable responses in recurrent glioblastoma, the patients invariably progress.” She and her team hypothesized that to be more effective, it was necessary also to block VEGF receptor signaling. They did so by combining bevacizumab with sorafenib, another targeted drug.

The team has also combined bevacizumab with dasatinib, a smart drug that helps block tumor cell invasion. They developed this combination because glioma cells in a significant percentage of patients escape the effects of bevacizumab and invade the brain to establish new tumors in distant sites. Both this combination and the bevacizumab-sorafenib combination are now in clinical trials through the NCCTG.

Another drug combination currently being tested through NCCTG includes the use of vorinostat with bortezomib. Vorinostat interferes with the coiling of a tumor’s genetic material and has shown single-agent activity in patients with recurrent glioblastoma. It is hoped that this drug combination will further enhance this benefit.

Adds Dr Galanis, “In many of our trials, we give the therapy before scheduled surgery so we can examine the effect of the drug on the tumor itself. In all our trials, we try to correlate the baseline tumor specimens with their genetic characteristics and the patient’s outcome to predict who will get the most benefit from the drug.”

Supported by the extensive in-house infrastructure that molecular and gene-based investigations require, researchers like Dr Galanis and colleagues across Mayo’s 3 sites can collaborate in developing therapies, analyzing clinical outcomes, and conducting laboratory reassessments. In this way, they have generated novel drug combinations and pioneered novel therapies like oncolytic virus therapies and targeted drug combinations for expeditious entry into new clinical trials.

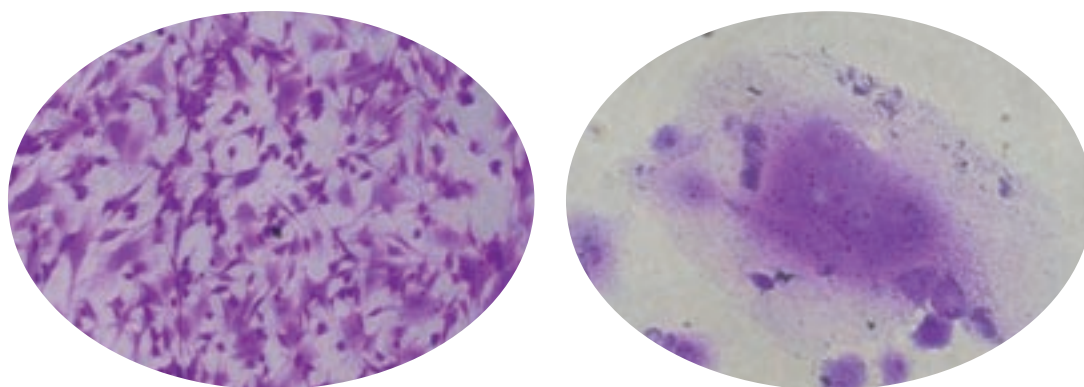


Figure. Infection with measles vaccine strain derivatives results in prominent syncytia formation in primary glioma cells. Extensive syncytia formation is observed preceding cell death (A, uninfected; B, infected).

Research Highlights

Diffusion Tensor Imaging Characteristics of Amnesic and Nonamnesic Mild Cognitive Impairment

The data generated by this imaging technology may be helpful in differentiating between various forms of dementia and cognitive impairment in the future. This study was presented at the Alzheimer's Association International Conference on Alzheimer's Disease in July 2009. Authors, all from Mayo Clinic: K. Kantarci, R. T. Avula, M. L. Senjem, A. R. Samikoglu, M. M. Shiung, S. A. Przybelski, S. D. Weigand, H. A. Ward, P. Vemuri, D. S. Knopman, B. F. Boeve, R. C. Petersen, C. R. Jack Jr.

Predicting Alzheimer's Disease

The clinical criteria for mild cognitive impairment are better at predicting who will develop Alzheimer's disease than a single memory test. This study was presented at the Alzheimer's Association International Conference on Alzheimer's Disease in July 2009. Authors, all from Mayo Clinic: R. C. Petersen, D. S. Knopman, B. F. Boeve, R. Cha, V. S. Pankratz, Y. E. Geda, R. O. Roberts, C. R. Jack Jr.

Racial Differences in Primary Central Nervous System Lymphoma Incidence and Survival Rate

A new study that shows the incidence of primary central nervous system lymphoma (PCNSL) is 2 times higher in black Americans, aged 20 to 49 years, than in white Americans. This study was published in the June 2009 issue of the *Journal of Neuro-Oncology*. Mayo authors: J. S. Pulido, R. A. Vierkant, J. E. Olson, B. P. O'Neill.

Differential Diagnosis of Neurodegenerative Dementias Using Structural MRI

This study was presented at the Alzheimer's Association International Conference on Alzheimer's Disease in July 2009 and showed that STAND-Map of each dementia syndrome in pathologically confirmed cases is unique and may be useful for differential diagnosis of new incoming subjects. The proposed framework establishes a direct relationship between a structural abnormality biomarker (MRI) and the "gold standard" of pathology. This information is then incorporated to provide differential diagnosis in new incoming dementia patients. Authors: P. Vemuri, K. Kantarci, M. L. Senjem, J. L. Gunter, J. L. Whitwell, K. A. Josephs, D. S. Knopman, B. F. Boeve, T. J. Ferman, D. W. Dickson, R. C. Petersen, C. R. Jack Jr.

Disrupting Disordered Neurocircuitry: Treating Refractory Psychiatric Illness With Neuromodulation

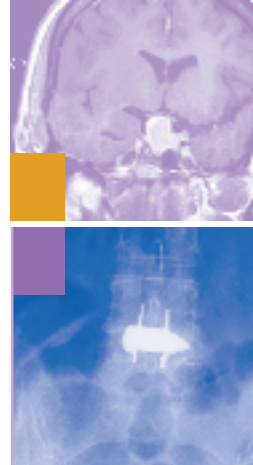
This review article addressing the use of deep brain stimulation for treating depression, obsessive-compulsive disorder, and Tourette syndrome appeared in the July 2009 issue of *Mayo Clinic Proceedings*. Author: K. H. Lee.

Previous Exercise Helps Stroke Patients Recover Faster

Stroke patients who had previously exercised regularly before a stroke occurred were significantly more likely to have milder impairments and, thus, were better able to care for themselves, compared with patients who rarely exercised. This multicenter study appeared in the September 2009 issue of *Journal of Neurology, Neurosurgery & Psychiatry*. Mayo authors: D. N. Stroud, T. M. L. Mazwi, R. D. Brown Jr, T. G. Brott, J. F. Meschia, for the Ischemic Stroke Genetics Study Investigators.

Mayo Clinic Identifies 2 Genes as Potential Therapeutic Targets for Multiple Sclerosis

This Mayo Clinic study found that 2 genes in mice were associated with good central nervous system repair in multiple sclerosis (MS). The research suggests that there may be a small number of strong genetic determinants for central nervous system repair following demyelinating disease, rather than a larger number of weak determinants. These findings give researchers new hope for developing more effective therapies for patients with MS and for predicting MS patients' outcomes. This study was presented at the Congress of the European Committee for Treatment and Research in Multiple Sclerosis in Dusseldorf, Germany, on September 11, 2009. Researchers included A.J. Bieber, PhD, M. Rodriguez, MD, and K. Suwansrinon, MD.



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

New Ways of Monitoring and Treating ALS



Kevin B. Boylan, MD

Although there is no cure for amyotrophic lateral sclerosis (ALS), therapies to slow disease progression are in clinical trials. The question of how to measure the effects of therapeutic intervention is critical. Generally accepted measures—assessments of physical strength and muscle function—lack precision and can require 6 to 12 months to give reliable results. Neurologist Kevin B. Boylan, MD, and colleagues at Mayo Clinic in Florida are working to develop a more reliable test.

Their goal is a peripheral blood test that could be used to monitor the rate of nerve fiber loss in ALS by measuring the presence of a biomarker—a neurofilament subunit or protein called pNF-H, which helps maintain the structure and shape of nerve fibers. It is released as motor axons break down. Previous studies have shown that levels of pNF-H are elevated in the cerebrospinal fluid (CSF) of ALS patients and that increasingly elevated levels correlate with patients' decline. However, because serial lumbar puncture is not practical for routine monitoring, Dr Boylan and colleagues hoped to develop a less invasive test.

Using a new monoclonal antibody and enzyme-linked immunosorbent assay (ELISA), they found that levels of pNF-H were elevated 2.8-fold in the circulating blood of ALS patients compared to healthy adults. Now they are investigating how well blood levels of pNF-H correlate with disease progression and with pNF-H levels in the CSF of a group of ALS patients. If results continue to be promising, the test will be developed for a larger trial. Such a

test would not only improve monitoring the effects of therapy, but also might offer a way to estimate the rate of progression in ALS.

Clinical Trials for Novel Interventions

Dr Boylan and his colleagues are also conducting clinical trials on several novel therapies.

Drug Studies

A drug being tested for its effectiveness in slowing ALS progression is the antibiotic ceftriaxone. Ceftriaxone is being evaluated in ALS because research suggests that it may reduce levels of glutamate near motor neurons, believed to be a factor in motor neuron loss in ALS. This study is currently open for enrollment.

Another drug, a combination of dextromethorphan hydrobromide

and quinidine sulfate, has shown promise in modulating pseudobulbar affect (inappropriate laughing and crying) in people with ALS. Trials are under way to determine the optimal dose.

Diaphragm Stimulation Study

Not to be confused with a respiratory aid or pacemaker, a new diaphragm pacing stimulation device (Figure) is intended to delay the decline of pulmonary function in ALS. An external electronic stimulator, attached to 4 wires implanted in the diaphragm, conditions the diaphragm by stimulating nerve fibers in the muscles so that they can function more effectively in the face of nerve fiber loss. Patients use it for fixed intervals several times a day. "The hope is that electronic stimulation to exercise the diaphragm will delay the point at which mechanical ventilation is needed," Dr Boylan explains. Mayo Clinic is 1 of 10 US centers engaged in the study of 100 patients. Enrollment is complete and the patients are being monitored.

Clinical Care: Mayo's Designated ALS Association Centers

Dr Boylan is the director of the ALS Clinic at Mayo Clinic in Jacksonville, Florida. Like Mayo's other 2 ALS clinics in Rochester, Minnesota, and Phoenix, Arizona, it is an ALS Association (ALSA)–designated Center of Excellence. Through its center program, ALSA "selects, certifies and supports distinguished regional institutions recognized as the best in the field" as centers with experience and knowledge of ALS, neurologic diagnostics and imaging, and on-site licensed and certified ancillary services. The service providers at all 3 Mayo sites include neurologists, nurses, physical, occupational, and respiratory therapists, dietitians, psychologists, social workers, and speech-language pathologists.

"The aim of the ALS clinical centers is to bring together key care providers so that each patient is monitored several times a year by the entire team," notes Dr Boylan. A comprehensive set of recommendations, arrived at in a team meeting, is communicated to the patient and to providers, physicians, and medical equipment suppliers in the patient's community. He adds, "Our clinics deal with all aspects of care—mobility, respiration, assistive communication, nutrition, and swallowing for the patient and social and psychological support for both patients and families."

As Mayo researchers continue to test new drugs, search for critical biomarkers and genetic mechanisms, and develop more precise means of monitoring response to therapy, the ALS clinical centers across Mayo continue to provide patients with intensive team care, focused on improving quality of life and slowing disease progression.



Figure. An external electronic stimulator, attached to 4 wires implanted in the diaphragm, conditions the diaphragm by stimulating nerve fibers in the muscles so that they can function more effectively in the face of nerve fiber loss.

Virtual Spine Clinic

Evaluating Patients Before They Arrive

For the past 7 years, an interdisciplinary team at Mayo Clinic in Arizona has been conducting a virtual spine clinic, a prescreening process for spine problems that has saved many patients an unnecessary trip to Mayo and has expedited evaluation and treatment for numerous others whom Mayo can help. Unlike the standard telephone consultation, the virtual spine clinic is a regularly scheduled, interdisciplinary team conference in which the patient's medical record, imaging studies, and patient-provided data are pre-reviewed by physicians from neurosurgery, physical medicine, and pain anesthesiology.

Reviewing 30 to 40 cases every other week, the participating physicians have served thousands of patients. The conference is reserved for cases in which the condition and/or the potential benefits of further evaluation or treatment are complicated or equivocal. The patients are from outside the immediate Phoenix area. Most of them have had prior treatments; many, but certainly not all, are self-referred. Decisions are made on the day of the conference.

If the team agrees that a visit to Mayo Clinic may benefit a patient, the patient is prescheduled for the necessary tests and consultations to smooth the process of evaluation and treatment. As Barry D. Birch, MD, the neurosurgeon who initiated the conference, notes, "Our goal was to streamline care and to make the patient's encounter at Mayo as efficient as possible."

The other goal is to be sure that for patients coming from a distance, the trip is worth their while. If it is decided that Mayo Clinic does not have anything new or different to offer, that conclusion is also conveyed to the patient and/or referring physician. Patients who decide on that basis not to come are usually grateful for the savings in time and expense and appreciative of the fee-free, multidisciplinary consultation.

Patient Input: The Spine Encounter Form

Before the virtual conference, patients are asked to provide relevant records and imaging studies that are entered into Mayo's system for digital review. They also fill out a Spine Encounter Form, which details the symptoms they are experiencing, the treatments they have had, and what they hope to gain from an evaluation. The form includes a diagram on which they can mark areas of pain. It provides a key piece of the puzzle. As Matthew A. Butters, MD, head of physical medicine and rehabilitation, puts it, "The diagram lets us see if the patient's pain matches the imaging studies. In addition,



Barry D. Birch, MD, and Mark K. Lyons, MD

conditions that may benefit from surgery often have a classic distribution of pain, so it helps us determine the options."

Enhancing Practice Integration

As neurosurgeon Mark K. Lyons, MD, notes, many people with back pain hope for a surgical cure. "At Mayo," he says, "we take a measured approach to spine care. We feel it serves the patient's best interest to proceed from a conservative approach to a more aggressive one, and the integrated practice allows us to do that."

Enhanced practice integration is one of the advantages of the virtual spine clinic. On a case-by-case basis, it has helped to educate participating physicians not only about which patients might benefit from a given specialty, but the nature of the benefit. Gathering around a table, reviewing cases and sharing thoughts, has translated into a better understanding of what each discipline can offer. For example, if a patient is determined not to undergo surgery, the potential benefits of physical therapy, pain medication and injections, acupuncture, and behavioral interventions such as relaxation training and biofeedback can be reviewed by physiatrists and pain anesthesiologists during the conference. Similarly, neurosurgeons can delineate the reasons why a given patient's condition may or may not improve with surgery.

Dr Butters finds that improved efficiency goes beyond the conference cases into his general practice. "Patients who are not specifically seeking a neurosurgical consult usually come through the Department of Physical Medicine and Rehabilitation. Having spent a great deal of time in the virtual spine clinic with the neurosurgeons, I have a better feel for what



Matthew A. Butters, MD

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neurosurgery can offer and can then communicate that directly to the patient."

David M. Rosenfeld, MD, a pain anesthesiologist, agrees: "We all work closely together, often seeing the same kinds of patients. The conference helps us channel patients in the right direction." He goes on to say, "It has been a good way to appreciate how other specialties approach a problem. Prescreening may not be that rare in other institutions, but this type of prescreening, with 3 disciplines sitting around the table, offering input, is."

As Dr Birch sums up, "The virtual consultation brings everyone involved in spine care together so we have a collaborative

interpretation of a patient's problems before the patient arrives at Mayo."

At a time when health care is increasingly costly and there is increased pressure on limited resources, the virtual spine clinic represents a model of off-site health care delivery, improving the practice, enhancing efficiency, and providing benefits to both patients and physicians.



David M. Rosenfeld, MD



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