

## A Rare Disorder, Ripe for Research

Clinicians and investigators join forces and take on transverse myelitis.



**Cody Unser raises funds to support research in transverse myelitis, the disease that came on “out of nowhere” when she was 12 years old.**

Its symptoms seem to know no bounds: Pain in the lower back, chest or neck. Legs that are numb. Hands that tingle. Headache. Fever. Loss of appetite. A general malaise. They can develop over a period of several weeks, hours—or, as one young woman, Cody Unser, recalls, even minutes.

“I was 12 years old. I was playing on the basketball court. Out of nowhere I had a hard time catching my breath, and I had a really big migraine. This all happened within the span of 20 minutes. They laid me down in the locker room. My left leg went numb. My right leg was tingling. And that was the last time I ever walked.”

Unser was diagnosed with transverse myelitis, a rare neurological disorder caused by inflammation of the spinal cord that can leave victims permanently disabled. Now 20, Unser is paraplegic, but leads an active life. The daughter of retired race car driver Al Unser Jr., she runs her own foundation, advocates for stem cell research, and takes part in fund raising for the Johns Hopkins Transverse Myelitis Center and Project RESTORE (see sidebar).

TM is one of a group of disorders in which the

immune system becomes abnormally activated and attacks the nervous system. The attack can damage or destroy myelin, the fatty insulating substance that covers nerve cell fibers, interrupting communication between the nerves in the spinal cord and the rest of the body.

TM is rare—only about 1,400 cases are diagnosed in the United States each year. But because it is “monofocal,” meaning it affects just one region of the central nervous system, and “monophasic,” meaning the attack occurs just once, it lends itself particularly well to the study of novel neuro-protective and -restorative therapies.

Faculty and staff at Hopkins’ TM Center, the only clinical and research enterprise of its type in the world, are dramatically improving the treatments and care of TM patients. “Aggressive treatment during the first three months is critical for better recovery,” says Douglas Kerr, the clinician scientist who directs the TM Center.

Kerr is testing two potentially effective treatments: the blood hormone erythropoietin and the anti-inflammatory drug thalidomide. A clinical trial of erythropoietin now is enrolling participants. A trial of thalidomide is planned for the near future. ■

### Project RESTORE

They’re both inflammatory disorders of the central nervous system. In both, the immune system becomes abnormal and attacks the nervous system. And now, transverse myelitis and multiple sclerosis are the focus of Johns Hopkins Project RESTORE, a research initiative that aims to rapidly develop new diagnostic and therapeutic strategies for these two debilitating diseases.

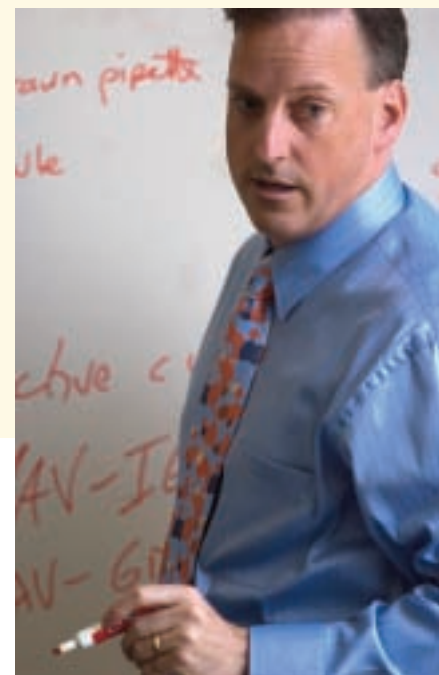
Already the Hopkins team has identified novel strategies that allow the nervous system to withstand immunologic attack. From stem cells, they have generated thousands of new motor neurons in the spinal cords of paralyzed animals. What’s more, they’ve stimulated these neurons to extend axons out toward muscle.

Strategies like these will be applicable to Alzheimer’s disease, Parkinson’s, traumatic spinal cord injury and stroke. And, says project director Douglas Kerr, for patients with longstanding paralysis, they represent the only hope for restoration of function.

RESTORE researchers develop and maintain extensive clinical databases on TM and MS patients. Using novel robotic and computer technology, they screen tens of thousands of drugs individually and in combination to see how they affect the cells involved in degenerative insults that mimic the injury in the human disease.

When diseases are rare, it is often difficult to obtain funding from the National Institutes of Health to pursue new research questions. Fortunately for Project RESTORE, donors are providing much of the philanthropic support necessary to advance its scientists’ discoveries.

Info: Chitra Krishnan, executive director, Project RESTORE, 410-955-3129, [restore@jhmi.edu](mailto:restore@jhmi.edu), [hopkinsneuro.org/restore](http://hopkinsneuro.org/restore)



**Douglas Kerr oversees Johns Hopkins’ innovative transverse myelitis and multiple sclerosis research initiative.**

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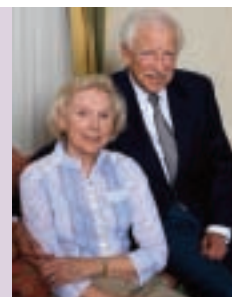
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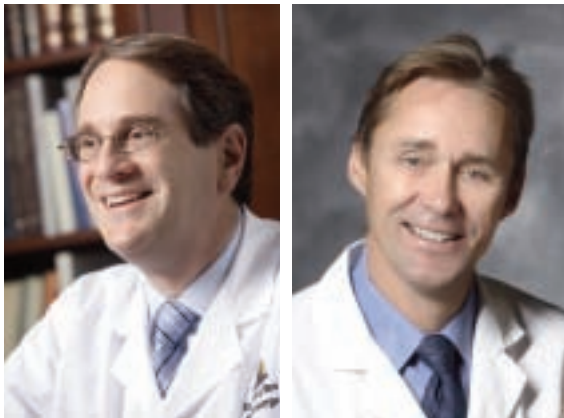
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Henry Brem

Justin McArthur

In this time of tremendous excitement in the neurosciences, we are exceptionally fortunate to have the right people in the right place at precisely the right time in science to translate the important discoveries now taking place into improved patient care.

Deep brain stimulation, for example, highlighted in this inaugural issue of *NeuroNow*, is a surgical treatment principally for Parkinson disease, and Johns Hopkins has long been a leading center for DBS. Now investigators suspect that the technique holds tremendous promise for conditions as diverse as refractory depression, obesity, Tourette syndrome and obsessive compulsive disorder. But we want to systematically study and introduce these powerful new treatments in a responsible manner. To do so, our physicians cannot rely on clinical reimbursements alone.

Nor can our scientists rely on shrinking National Institutes of Health dollars. Our young investigators, in particular, who are making the jump from residency training to junior faculty, need to establish their clinical research programs, but without a proven track record of publications, they often face repeated rejections when applying for NIH grants. Some, no doubt, will be tempted to abandon academic medicine altogether. In the Department of Neurology we will endow a discovery fund which will help support—and retain—these talented young scientists who will help us translate neuroscience discoveries into effective treatments.

It's also a time of unprecedented growth. With six new faculty in pediatric neurosurgery, brain tumor and spine surgery, our Department of Neurosurgery now is one of the largest academic programs of its type in the country. In these areas, as well as in vascular neurosurgery, where new therapies for aneurysms and subarachnoid hemorrhage continue to be developed, breakthroughs are taking place at breathtaking speed.

But these innovations might never have been realized without the support of our many friends and donors. Each and every contribution, no matter how small, brings us closer to our goal of improving outcomes in neurologic disease.

Henry Brem,  
Harvey Cushing Professor and Director of Neurosurgery

Justin McArthur,  
Interim Director of Neurology

## Unmasking the Mystery of Myositis

**M** yositis is a painful, debilitating muscle disease in which the immune system attacks healthy muscle tissue. Its chief symptom is muscle weakness, but because it so closely resembles other diseases, it's difficult to diagnose. In fact, most patients see as many as six doctors, on average, before they get a proper diagnosis.

Tamika Moore's primary care doctor believed she had liver disease. The 26-year-old physical therapist on staff at Johns Hopkins was inexplicably weak. When a blood test showed elevated liver enzymes, a gastroenterologist scheduled her for a liver biopsy. A second blood test, though, showed abnormally high amounts of the muscle enzyme creatine kinase, an indicator of muscle disease.

Moore's next stop? The Myositis Center, where specialists in muscle disease, including neurologists, rheumatologists and a pulmonologist, treat adults with all forms of the disease: polymyositis, which sometimes affects the lungs; dermatomyositis, which is often accompanied by a skin rash and is linked to a high rate of cancer; and inclusion myositis, an inherited form of the disease.

Patients undergo a battery of

tests, most often electromyography (EMG) to assess the health of the nerves controlling the muscles, muscle MRI, CT scans and pulmonary function tests. All can usually be done in one visit.

Patients are treated medically with drugs, especially corticosteroids. "A significant fraction go into remission. A second group continues treatment with some sign of disease. A third group," says center co-director Andrew Mammen, "is difficult to help, but you keep trying."

Center co-director Lisa Christopher-Stine is collecting information from large numbers of patients to help determine optimal treatments. "Now," says Mam-

men, "we have a grab bag of medicines, but we can't predict which patient will be most helped by which medicine."

One of the center's strengths is that it is jointly led by a neurologist, Mammen, and a rheumatologist, Christopher-Stine. "That's unusual because with autoimmune disease, neurologists and rheumatologists don't always see eye to eye," says Mammen. "Neurologists think rheumatologists are poor at diagnosis; rheumatologists think neurologists are poor at using medicines to treat immunosuppression. Lisa and I, though, have none of those hang-ups. We're learning from one another."

*Appointments: 410-550-6962.  
Info: [hopkinsmedicine.org/myositis](http://hopkinsmedicine.org/myositis)*

### Passano Physician Scientist Award

Andrew Mammen is investigating the link between dermatomyositis and cancer, research that could yield insights into the role the immune system plays in the development of tumors and in cancer itself. So critical is the research that Mammen, co-director of the Myositis Center, was recognized last year with a School of Medicine Clinician Scientist Award.

This year he was honored with a 2007 Passano Physician Scientist Award, given by the Passano Foundation to support the research activities of young clinicians. The Baltimore-based foundation has since 1946 annually also recognized outstanding senior investigators conducting research anywhere in the United States. More than 20 of these "Passano Foundation laureates" have gone on to win a Nobel Prize.

"Our mission is to encourage medical research with near-term clinical applications," says foundation chairman E. Magruder "Mac" Passano, who has involved his wife and three daughters in the foundation. "It's been exciting for us to get to know the award recipients and be a part of breakthrough medical research." ■

**Andrew Mammen and Lisa Christopher-Stine direct a center dedicated to myositis, a rare muscle disease that may hold clues to the immune system's role in cancer.**



# Deep Brain Stimulation for Movement Disorders—and More

**P**arkinson's disease is caused by a deficiency of dopamine, a chemical that transmits signals between nerve cells. In 1988, when a Hopkins team discovered that the deficiency led certain brain cells to be over-stimulated, not under-stimulated as was previously believed, it became clear that overactive cells could be addressed surgically. In 1997, deep brain stimulation, or DBS, a procedure that had almost disappeared after the introduction of the drug L-dopa around 1965, was approved in the United States for movement disorders.

Now DBS is a standard of care for Parkinson's, but it also has broad implications for conditions as diverse as obsessive compulsive disorder, obesity and psychiatric disease. Johns Hopkins, with its team of neurosurgeons and fellowship-trained neurologists, is a leading center for DBS in the United States and well positioned to pursue these powerful new treatments.

In DBS, a thin insulated wire, or electrode, is inserted through a small opening in the skull and positioned within the targeted brain area, usually, in Parkinson's patients, the subthalamic nucleus, a tiny midbrain structure. As with a cardiac pacemaker, an insulated wire is passed under the skin and connects the electrode with a neurostimulator, a battery-run power pack implanted under the skin usually near the collarbone. The generator sends a steady stream of low voltage to the brain, blocking the electrical signals that cause symptoms.

Hopkins neurosurgeon Frederick Lenz was instrumental in reintroducing DBS to neurosurgery after its hiatus. He refined microelectrode recording, an extraordinarily sensitive brain-mapping system which, in DBS, allows surgeons to precisely target specific groups of brain cells.

Lenz and his team have performed more than 400 DBS procedures. "While DBS was once used only in relatively advanced cases of Parkinson's, we are now taking patients earlier in the course of the disease," he says.

In Lenz's hands, involuntary movements improve significantly in 90 percent of patients. Gait improves in 70 percent to 80 percent. "Almost everyone gets at least a 50 percent reduction in medicine; some can stop taking their drugs completely," says Lenz. "The risk of infection is 1.5 percent. The risk of a bleed is 1.5 percent. Of that group, less than 1 percent will have a serious hemorrhage. It's up to the patients to decide whether the problems are significant enough to take the small but present risks of the procedure in order to achieve those results." ■



**Fred Lenz evaluates Parkinson's patient Martha Kowal to see if she is a candidate for deep brain stimulation.**

## DBS for Depression?

Over the last decade, deep brain stimulation has proven so successful in relieving the symptoms of Parkinson's disease that clinicians now are casting their eye on other areas that hold promise for this increasingly popular surgical procedure.

DBS has been done experimentally elsewhere on a small number of patients with treatment-resistant depression. The results so far have been promising, and though there has yet to be a definitive randomized study, the concept remains an exciting possibility.

"With movement disorders, we had great preliminary data, we had strong evidence for the target of the procedure, we had the failure of optimal drug therapy," says neurosurgeon Frederick Lenz, referring to levodopa, the drug many Parkinson's patients develop a resistance to. "In depression, these lines of evidence are less clear.

"However, neuroscience is advancing at a very rapid pace. I don't doubt that within a few years, implantation of DBS electrodes in patients with psychiatric disease could be the standard of care for depression that is refractory to medical treatment." ■

## NEW TO THE TEAM

### Pediatric neurosurgeon **Edward Ahn**

In fall 2004, as part of his neurosurgery residency at the University of Maryland, Edward Ahn did a rotation at Johns Hopkins in pediatric neurosurgery. The experience led him to serve a fellowship in that highly specialized field at the Children's Hospital Boston, where he trained in some of the latest techniques.

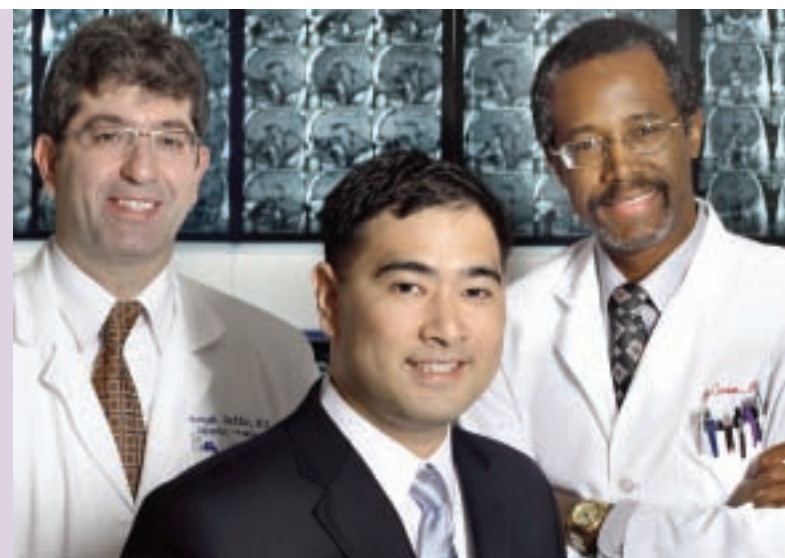
At the Children's Hospital Boston we had a high volume of children coming in from all over. When you're in a big center like that you become familiar with a wide range of pediatric neurosurgical procedures.

My special interests were congenital spinal cord anomalies, traumatic spinal cord injuries, epilepsy and craniofacial abnormalities, particularly craniosynostosis, a malformation of head shapes caused when the bony plates of the skull fuse together too early. To correct it, we often used a minimally invasive technique involving small incisions and far less blood loss. For most of our tumor cases, we used intraoperative MRI to ensure that there was adequate resection.

While I was in Boston, Dr. Jallo and Dr.

Carson invited me to consider working here. There was no question that I wanted to work with them and come back to Baltimore. I was born and raised here, and I had always dreamed of coming back someday and serving the city again.

The kids I operate on range from newborn on up. Some of my contemporaries would not choose that because they have young children of their own. My wife and I had our first baby during my fellowship, in fact, and every time I had an infant [patient], I could really feel what the par-



**In October, Edward Ahn, center, joined George Jallo and Ben Carson, left and right, on the pediatric neurosurgery service.**

ents were going through.

But I think being able to identify with parents is an added advantage. It makes you a better doctor because you really want to do the best for the children as if they were your own. ■

# Giving, While Living

**G**regory Riggins, director of neurosurgery research, has built a molecular biology laboratory dedicated to investigating new therapies for brain cancer, thanks to an endowed professorship.

On a special traveling fellowship, neurosurgeon Allan Belzberg flew to the Netherlands to observe a world-famous surgeon perform peripheral nerve surgery.

Neurologist Ted Dawson recently secured FPLC (fast protein liquid chromatography) for his movement disorders lab. The new equipment allows him to fully investi-

gate the major genetic cause of Parkinson's disease.

The professorship, the traveling fellowship and the lab equipment are but three of many gifts made by Florence and Irving Sherman over the last several decades, all with the express purpose of furthering neurological and neurosurgical research at Johns Hopkins.

Irving Sherman first came to Hopkins as a college freshman 65 years ago and then went on to medical school and residency training. "It was all Hopkins, all the way," says the 91-year-old retired neurosurgeon.

And though Sherman spent the better part of a long

career practicing in Connecticut, it was his training under legendary Hopkins neurosurgeon Walter Dandy from 1941 to 1943 that stands out as the experience of a lifetime.

A whiz-bang surgeon who was said to perform 1,000 operations a year, Dandy was dictatorial and demanding, but that did not dampen Sherman's admiration. "We residents did a tremendous amount of surgery. I was on duty constantly, night and day, 50 weeks out of the year. It was very hard work, but," Sherman adds wistfully, "it was wonderful."

Now the Shermans reside in Palm Beach, where each winter they take part in the annual Hopkins Medicine symposium, hosting luncheons and dinners that have raised millions for the institution. They travel frequently to Baltimore



**Florence and Irving Sherman:** "Give while you're alive. That way, you get to see the difference your gift makes."

PHOTOGRAPH BY ZUHAIR KAREEM



## Support for Students

These six Baltimore City high school seniors completed a summer internship designed for minority students in the Department of Neurology. Each intern received a \$3,000 stipend thanks to the generous support of friends of the department.

Neurology is also reaching out to the Student National Medical Association, the minority medical student organization. Thanks to a redesigned residency selection process, two-thirds of this year's incoming residents are under-represented minorities. ■

and to Hopkins, where he serves on the Council of the University President, the Johns Hopkins Medicine Alliance for Science and Technology Development, and the Department of Neurosurgery's advisory board.

The sheer joy the Shermans take in giving is palpable, and they have but one piece of advice for fellow Hopkins supporters: "Give while you're alive. When you give a bequest, you don't get the satisfaction of seeing how your gift benefits everyone. You don't get to see what happens." ■

## NeuroNow

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