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Induced Hypothermia Saves Lives in Neuro-ICU

Columbia and Weill Cornell doctors in the neurological intensive care units (neuro-ICUs) at NewYork-Presbyterian Hospital are bringing new hope to patients suffering from brain injury, stroke, cardiac arrest, and other devastating conditions affecting the central nervous system. Using cutting-edge neuromonitoring techniques and novel treatments such as induced hypothermia, patients who were once thought untreatable are now experiencing incredible recoveries.

"This specialty is about saving lives and recovering human beings to health who have, up until very recently, suffered the most severe and devastating form of medical illness we know," said Stephan A. Mayer, MD. "The conventional wisdom has been for decades that the brain can't recover. We have learned that a lot of that is wrong. The brain is resilient. Human beings can recover from brain injuries—people can recover from things that we never thought were possible. And neurointensive care really, at its heart, is about resuscitation."

"We practice goal-directed treatment of the brain," said Matthew E. Fink, MD. "We focus on what we have to do to maintain cerebral blood flow, oxygenation, get the brain adequate nutrients, and prevent swelling in the brain from causing secondary damage. When you focus efforts on what to do to save the brain, protect the brain, treat the brain—which is different from a lot of general ICUs which for the most part are focusing on heart, lungs, and kidneys—then it makes a big difference in patient outcomes."

The neuro-ICU at NewYork-Presbyterian Hospital/Columbia University Medical Center moved into a newly renovated space last year, and Dr. Mayer said that new equipment, such as a dedicated computed



tomography scanner and 3-tesla magnetic resonance imaging scanner, has dramatically improved their capabilities for both patient care and research. "We can obtain a diagnostic image of what's going on in ways that we were never able to do before," he said. "Every bed is wired for continuous [electroencephalogram] monitoring, and every room is wired with a dedicated multimodality system."

The neuro-ICU treats "every brain injury there is," Dr. Mayer said. "We treat intracerebral hemorrhage, putting thrombolytics in to dissolve the hemorrhage and remove it before it can cause damage. We helped pioneer a radical surgery called hemicraniectomy where you literally remove half of the skull for a massive stroke. It's all the rage now in Iraq, where a lot of soldiers are suffering brain

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Dystonia Research Sheds Light on Parkinson's

Researchers at NewYork-Presbyterian Hospital/Columbia University Medical Center—led by William Dauer, MD, of the Dauer Lab—are studying the link between disease gene function and brain mechanisms in motor system disease. The long-term goal is to identify novel therapeutic targets for motor system diseases.

Specifically, Dr. Dauer and his team are focusing their efforts on *DYT1* dystonia, the most common

genetic form of primary dystonia. "Unlike many neurologic diseases that are caused by neurodegeneration, such as Parkinson's disease (PD), dystonia, in contrast, appears to be a disease of abnormal motor circuit function," said Dr. Dauer. "So our hope is that if we can understand something about dystonia, we might deepen our understanding of the molecular and cellular mechanisms of motor behavior."

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Pregnancy and Epilepsy: Treatment Guidelines Revised

As of 2005, there were an estimated 1.1 million women of childbearing age with epilepsy in the United States. For women whose epileptic seizures are well controlled, evidence suggests that pregnancy, labor, and delivery pose a relatively low overall risk to the fetus as well as to the baby and mother, except in cases where valproic acid is used to help control seizures.

“In cases where women are very well controlled with the right medication, we don’t necessarily discourage pregnancy,” said Cynthia Harden, MD. “Only in cases where they are still having seizures, or if their seizures are being controlled with valproic acid, will we want to work with them to get the seizures under control or try to change to another antiseizure medicine before they get pregnant,” she said.

Dr. Harden, a member of the Technology and Therapeutic Assessment Committee of the American Academy of Neurology (AAN), and colleagues are currently revising the evidence-based practice parameter guidelines for the management of women with epilepsy who are planning to become or who are pregnant. The committee expects the new guidelines to be published in the AAN’s journal, *Neurology*, by the end of 2008.

“Preliminary analysis shows that valproic acid carries a high risk for major congenital malformations as well as some evidence of an association with adverse cognitive outcomes,” said Dr. Harden. She and members of the committee are working with the AAN to discourage physicians from prescribing valproic acid to women of childbearing age who want to become or who are pregnant.

“It’s relatively hard to find strong evidence for an increased risk in major birth defects with antiepileptic drugs (AEDs), except for cases in which women take valproic acid,” said Dr. Harden. “That being said, we still don’t have enough data for the newer AEDs, particularly those that may be good seizure-controlling alternatives to valproate, such as topiramate and levetiracetam.”

The need to gather information on AEDs as quickly and comprehensively as possible gave rise to the North American AED Pregnancy Registry, established in 1997 at Massachusetts General Hospital in Boston. Given the paucity of data and because the teratogenic risk of medications in humans

cannot be explored before a drug is launched, the registry’s major objective is to obtain and publish information on the frequency of major malformations, such as heart defects, spina bifida, and cleft lip, among infants whose mothers had taken one or more AEDs to prevent seizures or to treat any other medical condition.

Designated for pregnant women in the United States and Canada, the registry was established with funds provided by 6 companies that manufacture anticonvulsant drugs (Abbott, Eisai, GlaxoSmithKline, Novartis, Ortho-McNeil, and Pfizer). The research is conducted in a nonbiased academic setting to ensure that all findings

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—Cynthia Harden, MD

are purely evidence-based, with rigorous guidelines for release criteria, anonymity, and confidentiality.

“From the data we are seeing, it looks as though the standard AED medicines, such as carbamazepine, appear to be associated with the lowest risk. Moreover, the levels of carbamazepine during pregnancy are fairly stable. Since the levels of most AEDs decline during pregnancy, putting the patient at risk for seizures, it requires vigilance and a great deal of physician–patient communication to monitor the AED levels,” said Dr. Harden. “If a woman is stable on carbamazepine, evidence suggests there should be no contemplation of changing to another drug,” she added.

However, one of the problems in discouraging both patients and physicians from using valproic acid in women of childbearing age is that divalproex sodium (Depakote) is a very effective drug for controlling seizures, “and our primary goal in caring for people with epilepsy is to stop the seizures,” said Dr. Harden. “We really want seizures to be well controlled, especially for women who want to get pregnant.”

Enrollment in the AED registry requires a signed informed-consent document. Women are interviewed 3 times: at enrollment, at 7 months’ gestation, and 8 weeks after delivery.

“The patient has to contact the registry herself to give permission,” said Dr. Harden. “And whenever possible, women should call and sign up before they have their first ultrasound, so they’re not biased. If the first ultrasound is normal, they may decide they don’t need to sign up for the registry,” she said. Because women are receiving ultrasound testing earlier and earlier during the course of pregnancy, it becomes more challenging to register before their first ultrasound.

The mother’s written permission is also required before the exposed infant can be tested. The study dysmorphologist uses established inclusion/exclusion criteria to identify major malformations (defined as structural abnormality with surgical, medical, or cosmetic importance). The scientific advisory committee meets to anonymously review major findings. Findings in women who have enrolled before having any prenatal screening are used to decide when findings should be released.

The criterion for release of results for a positive association (relative risk, >1.0) is

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met when the lower value of the 95% confidence interval is 2.0 or higher. The release criterion for no associated increase in the frequency of all major malformations is met when the upper value of the 95% confidence interval does not exceed 2.0.

The external comparison group comes from the Active Malformations Surveillance Program at Brigham and Women’s Hospital, also in Boston. The findings in 69,277 newborns showed a baseline rate of 2.24%, which was reduced to 1.62% after excluding infants with genetic disorders and chromosome abnormalities.

The major malformations are identified between birth and 5 days of age. The inclusion/exclusion criteria are the same as those used in the AED Pregnancy Registry.

To enroll in the AED Pregnancy Registry, patients may call 1-888-233-2334 or visit the registry’s Web site at <http://aedpregnancyregistry.org/> for information. The registry is also recruiting participants for the control group by asking pregnant friends or family members who are not taking AEDs to enroll.

Contributing faculty for this article:
Cynthia L. Harden, MD

continued from **Dystonia**, page 1

When the Dauer Lab began conducting research on dystonia, torsinA, a protein, was known to be localized to the lumen of the main endoplasmic reticulum, but little else was understood about its biology. Dr. Dauer's team initially sought to determine the site of torsinA function within the endoplasmic reticulum/nuclear envelope system.

"It turns out there are a number of diseases that are caused by mutations of proteins that function in the nuclear envelope," he said. "To name just 2 [of them], mutations in the lamins cause an accelerated aging syndrome; other mutations cause neuromuscular disorders. But scientists are still at an early stage in the understanding of what actually happens in that nuclear envelope," he said.

In earlier biochemical studies in cell lines, Dr. Dauer concluded that torsinA does, in fact, play a role in the nuclear envelope. To test this finding in an in vivo setting, his lab created lines of genetically modified mice, which either lacked the torsinA protein or carried the exact human mutation in the mouse gene: a 3-base pair deletion simply deleting a single amino acid. Both lines of mice developed severe abnormalities of the nuclear envelope, confirming the in vitro results (*Neuron* 2005;48[6]:923-932).

Dr. Dauer noted 2 more important findings from the mouse studies: First, the nuclear membrane of the knockout mouse

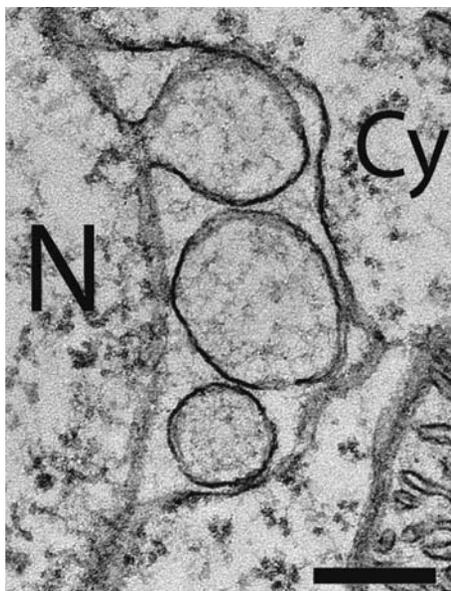


Figure. Detail of ultrastructure from torsinA mutant mice shows membranous blebs budding from the inner nuclear membrane which are pushing out against the outer nuclear membrane. Scale bar=300 nM. **Cy**, cytosol; **N**, nucleus.

looked exactly the same as that of the mouse with the disease gene mutation (Figure). "That told us that an effect of the disease mutation is to block the normal function of torsinA." Second, while the torsin protein is ubiquitously expressed in the body, nuclear membrane abnormalities in the mice only occurred in neurons. "Patients who have dystonia have torsin throughout their bodies; but when they get the mutation, they only get a neurologic disease, suggesting that what we are seeing may have some relation to dystonia pathogenesis," Dr. Dauer said.

The Dauer Lab is also investigating the relationship between the maturation of a neural stem cell into a neuron, its subsequent

"There are a number of diseases that are caused by mutations of proteins that function in the nuclear envelope."

—William Dauer, MD

migration and maturation into a circuit, and abnormalities in the nuclear membrane. "There appears to be something special about the neuronal nuclear membrane that occurs when neurons are maturing that requires the function of torsin protein that, for whatever reason, is not required by other cells," said Dr. Dauer. "This leads us to ask questions about the difference between a neuron and a non-neuronal cell, the features of a neuron, the changes that have occurred to the nuclear membrane of a neuron that are different, and why. And then we are inclined to ask, 'How might events at the nuclear membrane alter neuronal function?'"

In order to study what role, if any, torsinA may play in regulating the connections that exist between the nucleus and the cytoskeleton, Dr. Dauer is collaborating with Gregg Gundersen, MD, and Howard Worman, MD, both of whom direct labs at NewYork-Presbyterian/Columbia. The researchers are focusing on the connections that appear to be disrupted in a variety of diseases caused by mutations in nuclear envelope proteins. The Gundersen Lab, which recently made an important discovery about the role of fibroblasts in cellular polarization, is now using cells from torsinA knockout mice to identify abnormalities in nuclear movement, providing initial evidence that torsin is involved in the nucleo-cytoskeletal link. The findings may have important implications for how the brains of people with dystonia develop. The Worman Lab is exploring similar issues in relation to nuclear lamins.

"We have gone from a protein that we didn't know anything about to the idea that it has a special role in neurons; that the mutation of it wipes out this function, and that this function appears potentially to be involved in regulating the connections between the nucleus and the cytoskeleton," said Dr. Dauer.

In addition to studying abnormal motor circuit function, Columbia researchers are investigating the molecular mechanisms of neurodegeneration. Asa Abeliovich, MD, PhD, has been focusing on the degeneration of midbrain dopamine neurons that underlie PD. He and colleagues are working to make mature dopamine neurons

from stem cells, both from the point of view of basic science as well as the clinical application to PD. The researchers are particularly interested in uncovering the complex final steps of making a cell that can function as a dopamine neuron, and identifying the regulatory elements involved in the process.

"We have found 2 kinds of regulatory elements," said Dr. Abeliovich. "One is transcriptional regulators, and more recently we found another, more unusual class: short RNA molecules." Dr. Abeliovich's laboratory is also investigating dopamine neuron survival in a small number of genes representing rare genetic mutations linked to PD. "We are asking 2 questions," said Dr. Abeliovich. "First, 'How do these genes cause problems?' and a related question, 'Can these genes tell us anything about the normal function of dopamine neurons in motor behavior?'"

"In the 3 or 4 dopamine neurons we have studied, they seem to fit together in a couple of different pathways via a couple of different mechanisms," said Dr. Abeliovich.

The Abeliovich Lab uses human stem cell models to determine how the genes function in dopamine neurons, with an eye toward understanding what is wrong with the dopamine neurons that have the mutations associated with PD. Ultimately, the researchers are looking for replacement therapies for PD.

Contributing faculty for this article:
Asa Abeliovich, MD, PhD, and William Dauer, MD

New Alzheimer's Therapy Shows Promise in Phase III Trials

In a national Phase III study, Weill Cornell researchers at NewYork-Presbyterian Hospital are investigating the use of intravenous immunoglobulin (IVIg) for the treatment of Alzheimer's disease. The trial—led by Norman Relkin, MD, PhD—builds on preliminary studies showing that the deterioration in cognitive function that is typical of Alzheimer's disease slowed dramatically following treatment with IVIg. Among the small group of patients who participated in the original Phase I study and stayed in treatment, most retained their thinking abilities 3 to 4 years later, a period that is usually associated with significant decline in most patients with Alzheimer's disease.

“Not too much should be made of the small number of patients followed in our open-label study, but the initial results have certainly been very promising. I think it is fair to suggest that this is now one of the leading investigational Alzheimer therapies,” said Dr. Relkin. He noted that the National Institute on Aging awarded funding for the Phase III trial after his study proposal competed successfully against more than 50 other investigational Alzheimer's treatments.

In fact, there has been an explosion of interest in pharmacologic approaches to preventing, controlling, or reversing Alzheimer's disease, according to Dr. Relkin. He counted more than 30 clinical trials under way worldwide, with a spectrum of new agents using a variety of strategies.

Immunotherapy, which is the premise of IVIg, has been considered particularly attractive because of the experimental studies suggesting that β -amyloid, a peptide that forms the plaques that are a hallmark of the pathology, can be targeted by anti- β -amyloid antibodies. Although a commercial vaccine aimed at β -amyloid failed several years ago because of safety issues, this remains an important focus of research. “There are antibodies within IVIg that target oligomers, an amyloid aggregate that is directly toxic to brain cells.

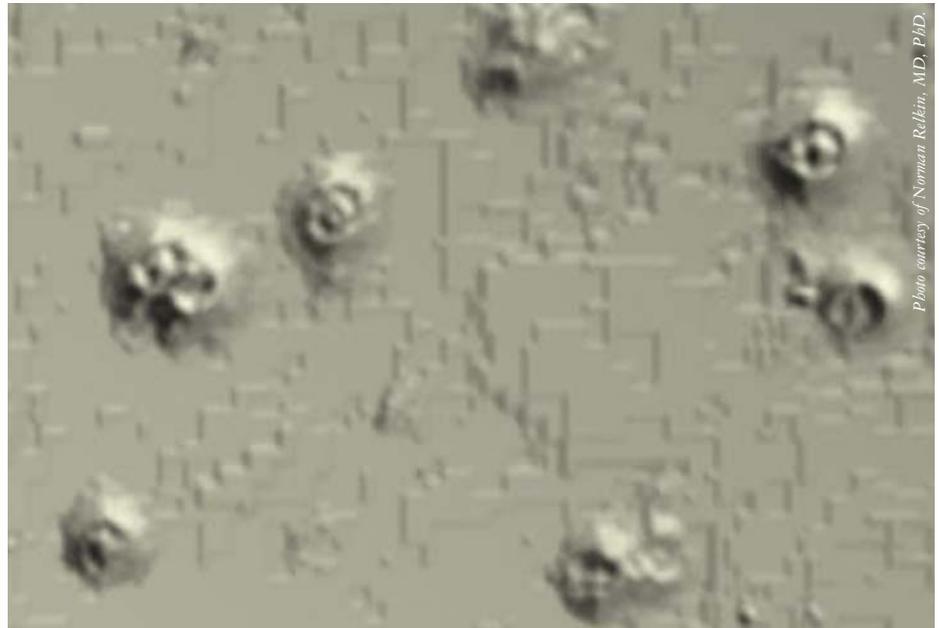


Photo courtesy of Norman Relkin, MD, PhD.

Digitally enhanced electron micrograph shows spherical oligomers. In Alzheimer's disease, β -amyloid oligomers cause damage to the brain; research shows they may be appropriate targets for treatment with intravenous immunoglobulin.

Oligomers may be closer to the actual cause of cognitive impairment in Alzheimer's than the amyloid plaques that were targeted by the earlier vaccine study,” Dr. Relkin said.

Dr. Relkin and colleagues presented interim results from the placebo-controlled Phase II trials with IVIg at the annual meeting of the American Academy of Neurology in April 2008. “The results provide further support for this approach and satisfy the preconditions for going forward with a large, multicenter Phase III study,” he said.

In the Phase III study, 36 to 40 centers are expected to recruit 360 patients who will be randomly assigned to receive either placebo or IVIg. The study will measure cognitive changes using standardized tests as well as global assessments of function over 18 months. A variety of secondary end points are also being monitored, including changes in cerebral metabolism and brain amyloid deposits as measured by positron emission tomography and brain morphology as measured by magnetic resonance imaging. The blood and spinal fluid will

also be examined with conventional and novel biomarkers, an area in which there has also been substantial recent progress.

“We have been involved for several years in a collaborative effort to identify proteomic markers in spinal fluid that can be used for the diagnosis of Alzheimer's. We are now testing much the same approach to monitor response to new Alzheimer therapies,” Dr. Relkin said. “We hope to learn whether IVIg is altering the biological processes that cause Alzheimer's disease, something that has not been proven to happen with currently approved treatments.”

Relative to other therapies being developed for Alzheimer's disease, one of the advantages of IVIg is that its safety record is already well established. IVIg, which contains pooled immunoglobulins extracted from plasma donors, has been used for almost 30 years for a broad number of indications, including some forms of cancer, idiopathic thrombocytopenic purpura, and primary immunodeficiencies. It has also been applied for many off-label uses, such as neuropathy and chronic fatigue syndrome, the latter because of the theoretical benefits of passive immunity against inflammation and low-grade infections.

However, IVIg is expensive and supplies are limited. “IVIg is a blood product, and there is concern about its supply if it does

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“We have been involved for several years in a collaborative effort to identify proteomic markers in the spinal fluid that can be used for the diagnosis of Alzheimer's [disease].”

—Norman Relkin, MD, PhD

Program Takes Innovative Approach to Pediatric Spasticity

Physicians and surgeons at Morgan Stanley Children's Hospital of New York-Presbyterian/Columbia University Medical Center are providing children with spasticity enhanced care and individualized treatment as part of a newly implemented multidisciplinary approach. Using treatment teams comprised of pediatric neurosurgeons, pediatric neurologists, orthopedists, physical therapists, occupational therapists, nurse practitioners, social workers, and specialists in bracing, the Hospital is offering children with these complex disorders an expanded arsenal of potential treatments. Often, numerous specialists are consulted as parents attempt to find the right combination of treatments to allow their child optimal function and quality of life, and the response to the program thus far has been overwhelming. The team is frequently asked to give talks to a variety of groups, including other health care practitioners and support organizations.

"Within 6 months, the waiting list had grown so long that we doubled the number of clinics to 4 times per month. This was clearly the right thing to do. These children have complex needs. Multidisciplinary care permits specialists to work together to provide more comprehensive solutions to problems," said Richard Anderson, MD.

More than 180 patients are now being

"At our Center, selective dorsal rhizotomy is performed with a physical and occupational therapist in the operating room."

—Richard Anderson, MD

followed by the team, and the number is growing. Typically, the specialists not only collaborate to determine the best approach to each patient's problem but also offer different aspects of care that together produce an optimal outcome.

For example, "one child may benefit from a tendon release to improve range of motion, but their ability to improve function may also depend on physical therapy or physical therapy in combination with pharmacologic therapy, such as Botox injections or muscle relaxants," said Dr. Anderson. "There is not usually just one solution."

A substantial proportion of the patients have cerebral palsy, but a broad spectrum of disorders can result in spasticity. Improving mobility and function may involve treat-



(Left to right): Dean Morgan, PT, Mary Maksomski, OT, and Claudia A. Chiriboga MD, MPH, examine a child in the spasticity clinic.

ments that address nerves, tendons, muscles, bones, or some combination of these. In certain cases, the specialists on the team are able to offer approaches that are not widely available. One of the procedures offered by Dr. Anderson is selective dorsal rhizotomy (SDR). All other centers in the tristate area perform SDR by removing 5 to 6 levels of bone. At the Morgan Stanley Children's Hospital, however, Dr. Anderson performs a minimally invasive SDR by removing only

one level of bone. According to Dr. Anderson, randomized clinical trials have shown that many children with spasticity benefit significantly from this operation.

"The procedure, guided by ultrasound, involves only a 1-inch incision at the bottom of the spinal cord," he explained. "At our Center, the procedure is performed with a physical and occupational therapist in the operating room. The therapists maintain contact with target muscles in order to help identify abnormal responses when an electrical stimulus of the nerve root is generated. This allows real-time physiologic feedback that provides intraoperative guidance on which nerve rootlets to cut."

Typically, the physical therapist has been working with the patient before the procedure

and is therefore intimately acquainted with the precise muscle targets. The goal of a multidisciplinary approach is to develop the most effective plan through the consensus of multiple experts. A variety of innovations have been made during the past couple of decades for the treatment of spasticity, and all are considered. For example, whereas intramuscular injections of botulinum toxin type A, which provides excellent but temporary muscle relaxation, may be sufficient for some individuals, others may need an implantable and programmable intrathecal baclofen pump, which delivers a muscle relaxant directly into the spinal fluid and provides continuous action.

"There are advantages and disadvantages to many of these options, and we work with children and their parents to identify an approach with which they are comfortable," Dr. Anderson explained. He emphasized that control of spasticity is the focus of the multidisciplinary clinic, but spasticity is often only one of several clinical issues that the team is equipped to handle. In general, spasticity cannot be cured, but its effects can be reduced in the context of comprehensive care that addresses concomitant health issues.

"Surgery can be an important component of treatment, but the [members of the] multidisciplinary team learn from each other about how to collaborate in addressing problems," said Dr. Anderson.

Contributing faculty for this article:
Richard Anderson, MD.

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in Iraq, where a lot of soldiers are suffering brain injuries. We do a lot of work now with epilepsy, and, of course, stroke.”

In addition, a newer type of patient is now treated in the neuro-ICU. These patients are victims of cardiac arrest. According to Dr. Mayer, even when the patient's heart is successfully restarted, the prognosis is grim due to severe brain damage from the lack of oxygen and blood flow

“The conventional wisdom has been for decades that the brain can't recover. We have learned that a lot of that is wrong. The brain is resilient. Human beings can recover from brain injuries—people can recover from things that we never thought were possible. And neurointensive care really, at its heart, is about resuscitation.”

—Stephan A. Mayer, MD

to the brain. He and colleagues are finding that induced hypothermia can “double or triple” the rate of survival in some patient groups (*Semin Neurol* 2006;26[4]:387-395).

“There's a subset of young people with the average age of 50 who have ventricular fibrillation, which is 25% of cardiac arrests,” he said. “With standard treatment, only 15% of these patients survive. If you cool those patients, 40% survive with good recovery.”

Dr. Mayer noted that induced hypothermia

is still seen as “new and unfamiliar.” He is working to change that view and encourage more hospitals to use it when treating cardiac arrest patients who may benefit from the treatment. “This treatment has to be available for everyone who is appropriate,” he said. “It's not good enough if you just happen to come in to the right hospital. We're leading an initiative throughout the whole NewYork-Presbyterian network where we teach neurocritical care. Induced hypothermia has potential risks and you need experience. We're working with the intensive care units in our hospitals so that they either learn how to do it or they transfer the patients to us.”

NewYork-Presbyterian doctors and nurses who work in other areas can join a rotation through the neuro-ICU, getting a sense of what they do and then bringing that knowledge back to the general ICU. In addition, the Neurocritical Care Society has

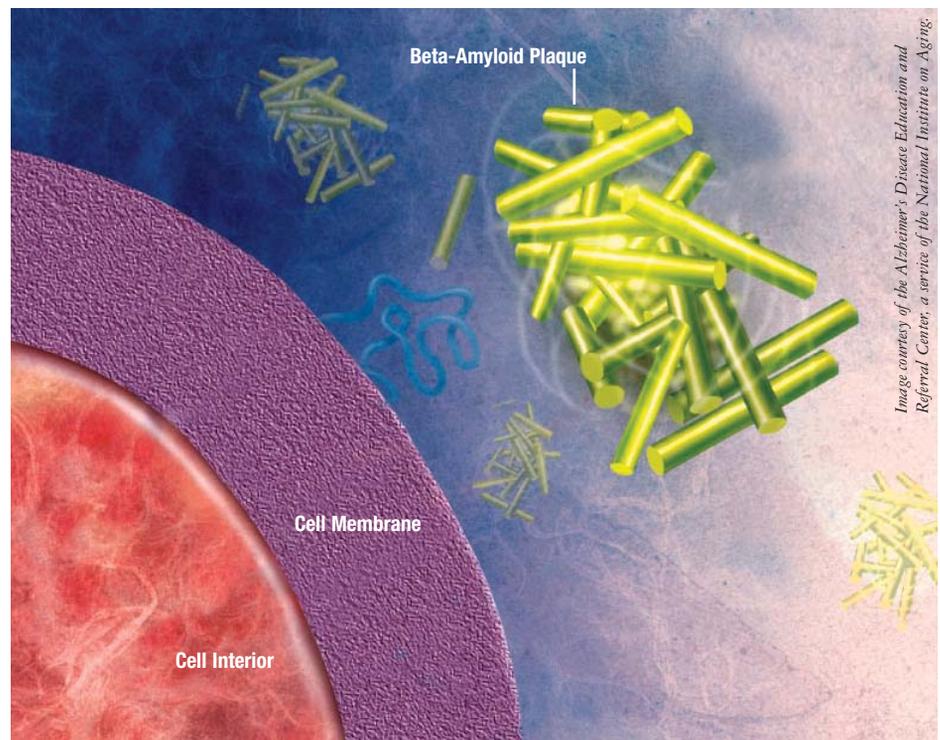
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prove to be effective in Alzheimer's disease, which is a highly prevalent disorder and a growing problem as the population ages,” Dr. Relkin observed. In anticipation of this, there are efforts under way to find replacements for IVIg and to produce the antibodies needed for treating Alzheimer's.

The need for new approaches to Alzheimer's disease is urgent. The only currently approved therapies target chemical deficiencies in the brain that are not considered to be the primary cause of the disease. In a number of studies, including those previously conducted by Dr. Relkin, these drugs have been shown to slow cognitive deterioration somewhat, but not sufficiently to prevent long-term decline. There are currently no approved therapies that can restore patients with this form of dementia to a normal state. Progress in understanding the biology of this disease has produced targets of interest for stopping progression, but Dr. Relkin cautioned that there are fundamental questions that have not yet been answered.

“Amyloid plaques and neurofibrillary tangles are the most well-described features of Alzheimer's. Some of the current trials are targeting plaques, but there are a number of reasons to believe that the plaques are not the direct cause of symptoms,” Dr. Relkin said. He indicated that despite the rapid advances in the understanding of Alzheimer's disease, the clinical trials will play an important role



An artist's rendering of β -amyloid plaque, the protein core of the brain plaques seen in patients with Alzheimer's disease.

in determining which aspects of this disease are treatable.

“IVIg is not the only agent in Phase III trials for Alzheimer's disease. Some of the drugs now in clinical trials are being tested in humans for the first time. History tells us that the majority of these agents will likely fail for reasons of safety or effi-

cacy. But even failures teach us more about Alzheimer's disease and how it might ultimately be defeated,” Dr. Relkin said. “This is how science and medicine move forward, and hopefully we're starting to move in the right direction.”

Contributing faculty for this article:
Norman Relkin, MD, PhD

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developed a subspecialty exam devoted to neurological intensive care and is accrediting a fellowship program at NewYork-Presbyterian Hospital; several doctors and nurses have already been trained specifically in neurological assessment and treatment.

"In my opinion, the most important factor in the treatment, survival, and recovery of these patients is exemplary nursing care," Dr. Fink said. "We have nurses who are trained in ways that go way beyond what most nurses do, and they are just absolutely spectacular."

Neurocritical care is an intense and demanding specialty, Dr. Fink said, but the rewards are well worth the effort. "What motivates us is the potential to help people who are at death's door," he said. "It just goes to show you that it is possible to treat these patients who in the past have been completely written off as being unsalvageable or untreatable. That's what keeps all of us going." Dr. Mayer agreed, adding, "I've seen 'hopeless' cases recover frequently enough that after 15 years in this business, I know less about prognosis than at any point in my career. The story of my career has been watching one unbelievably remarkable recovery after another."

Contributing faculty for this article:

Matthew E. Fink, MD, and Stephan A. Mayer, MD

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The following is a list of the doctors quoted in this issue of the *NewYork-Presbyterian Hospital Neuroscience Newsletter*. For more information on their work, please contact them at the e-mail addresses listed.

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