John (Jack) Hughes is the Reeve Foundation’s fifth Chairman of the Board since its inception in 1982 as the American Paralysis Association (APA). He follows Hank Stifel, Christopher Reeve, Dana Reeve and Peter Kiernan. Hughes has been a member of the Board since 2000; his family has been associated with the Reeve Foundation for over 25 years. After Jack’s brother Greg was spinal cord injured, Michael Hughes, their father, became involved with the Foundation and was for many years a board member. In 1999, the Hughes family made the largest-ever gift to the Reeve Foundation, enabling the organization to significantly expand its research program. Michael Hughes died in 2007. Greg remains active, chairing the Foundation’s Connecticut Chapter. Jack Hughes, CEO of Topcoder, the world’s largest competitive software development community in Glastonbury, CT, spoke with Reeve Foundation staff member Sam Maddox.

Q. In the early days when your family was thrown into the world of spinal cord injury, what was the sense of scientific progress?  
A. Almost 30 years ago, when my brother Greg was injured, spinal cord injury had a very dark prognosis – how could there be any progress at all if there wasn’t even anyone really working on the problem? The Reeve Foundation helped to change all that. Today we have a sophisticated research program that incorporates multiple initiatives and institutions and approaches, a very full research continuum. We helped build the Foundation out to the point now where it will take basic research and move it down a translational pipeline. We put the infrastructure in place for developing our North American Clinical Trials Network, for example, and the NeuroRecovery Network. We have built what I consider to be a world-class organization.

Q. So the Foundation is more broadly based than in the days when cure was the focus?  
A. Yes, that is right. Now, our efforts are based much more on our interaction with the community. We released our paralysis survey last year and found out there are many more people living with spinal cord

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Mary Bartlett Bunge, a distinguished scientist at the Miami Project, thought about retiring after 57 years at the bench. Last year, she decided not to participate in the three-year renewal proposal for the Reeve Foundation International Consortium on Spinal Cord Injury; she had solidified her plans to retire by the end of 2010. Her Consortium colleagues threw her what they thought was a retirement party. “Can I just say I’m not retiring?” says Dr. Bunge. “There is a graceful time to retire and I don’t think it’s quite as close as I thought it was. I’m just working, hopefully a little bit less.” She says she’s cut back to 75 percent. “I have a new postdoc in my lab. I’m continuing some studies because there are things that I still want to do and I still am energetic and have a passion to try and do something more.”

One of the loose ends Dr. Bunge wants to tie up is a pending clinical trial for spinal cord injury using a combination of treatments including Schwann cells, a type of support cell in the nervous system that she has studied over most of her career.

This article, then, is not a retirement notice. It is a tribute to Dr. Bunge and a thankful appreciation for her many years of work with the Consortium.

Mary Bartlett was interested in science at an early age. “I used to row a small leaky rowboat along a stream in front of our house and look at all the wildlife, particularly the tadpoles and the very tiny frogs. That inspired me to wonder how the development occurred from tadpole to frog.”

She might have been a fashion designer. “I used to design and make my own clothes before I went to college so fashion design was a possibility. I was also interested in child psychiatry but biology won out. I was thinking that’s something I cannot do on my own. I could make clothes on my own. But I could not get into biological studies on my own so I decided I needed training for that.”

After high school Dr. Bunge took college courses to become a laboratory technician. A summer course at Jackson Laboratories at Bar Harbor “changed the course of my life. One day we put rabbit heart muscle into tissue culture and I saw it beating. I didn’t want to be a technician. I wanted to get into research.”

Dr. Bunge went to graduate school at the University of Wisconsin, at the invitation of Dr. Robert Schilling. They worked on projects and published papers related to intrinsic factor and gastric juice. “I saw him recently. He’s now 90 years old, still working. He said that our papers published in 1956 and 1957 are still highly regarded. But I wasn’t really interested in gastric juice.” She received her masters in Medical Physiology.

“In the meantime I had taken this course in cell biology with Dr. Hans Ris and had looked at images in the electron microscope. That was another inspirational, defining moment. We were using one of the first electron microscopes in the United States; we had to hammer the lenses into place. But still the images were just captivating.”

As a graduate student Dr. Bunge took courses with medical students. This is where she met Richard Bunge. “There was this lanky looking guy. I used to sit in the front row and he sat in the front row at the other end. Then, for a summer Richard worked in Dr. Schilling’s lab, on blood samples in the cold room. I didn’t see him during the day. Then at 5 he would vanish into the hospital cafeteria where he washed dishes to help support himself while in medical school. I thought, this guy needs fresh air. I invited him to go sailing and that’s how we got to know each other. When the wind died down in the middle of Lake Mendota we had wonderful long conversations. Dick was going to medical school so he could be a missionary; his hero was Albert Schweitzer.”

Back on campus, Dr. Bunge began what was to be a lifelong collaboration with Richard, who had changed his mind about being a missionary in favor of research. Between getting her masters and her Ph.D., Mary and Richard were married. “He really introduced me to neuroscience. From grad school on, we worked together.” They demonstrated that myelin could be reformed in the mature mammalian spinal cord. “When I put a section of kitten spinal cord into the electron microscope, there in the first area of the first section I looked at,
was an image like the old fashioned ice tongs with the oligodendrocyte cell body at the top and two cytoplasmic arms coming off the cell body and it was forming myelin at the end of each arm. And that’s how I discovered that the oligodendrocyte was the cell that made the myelin sheath for the central nervous system. That was one of my big moments in research.”

Dr. Bunge says her husband became interested in nerve tissue culture and wanted to go to New York to study with Dr. Margaret Murray at Columbia. “She helped develop the techniques for nerve tissue culture and was able to achieve myelination in culture.” Fortunately, there was an electron microscopy lab at Columbia headed by Dr. George Pappas. Very little work had been done to look at the detail in these tissue cultures. “Again we were looking at myelination; actually Dick and I were the first to describe synapse formation in tissue culture.”

In New York the Bunges had two sons, Jonathan and Peter. Mary Bunge continued part time in the lab. The family left Columbia in 1970 for Washington University School of Medicine in St. Louis. Dr. Bunge was interested in nerve tissue culture and wanted to separate the cells in the peripheral nervous system. With Dr. Patrick Wood, we could grow neurons by themselves, the Schwann cells by themselves or the fibroblasts from peripheral nerve by themselves. Then we could prepare different combinations and observe a number of important interactions that occur between these cells, not possible in an animal.”

Much of the work in St. Louis was directed toward multiple sclerosis, which is characterized by myelin loss. “Even though Dick and I were really basic scientists, we always were interested in how we could translate — that word wasn’t used at that time — how we could extend our basic science results to help repair a deficiency or degeneration in the central nervous system.”

The Bunge lab continued in the area of myelin repair. Says Dr. Bunge, “Rather than take a piece of tissue and try to see how much differentiation we could achieve, the Margaret Murray approach, we wanted to separate the cells in the peripheral nervous system. With Dr. Patrick Wood, we could grow neurons by themselves, the Schwann cells by themselves or the fibroblasts from peripheral nerve by themselves. Then we could prepare different combinations and observe a number of important interactions that occur between these cells, not possible in an animal.”

The combination strategy, much of it in collaboration the Reeve Foundation Consortium, is more effective than Schwann cells alone. Says Dr. Bunge, “Rather than take a piece of tissue and try to see how much differentiation we could achieve, the Margaret Murray approach, we wanted to separate the cells in the peripheral nervous system. With Dr. Patrick Wood, we could grow neurons by themselves, the Schwann cells by themselves or the fibroblasts from peripheral nerve by themselves. Then we could prepare different combinations and observe a number of important interactions that occur between these cells, not possible in an animal.”

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The Bunge lab at the University of Miami became one of the preeminent SCI labs in the world. In 1993 Richard Bunge was invited to join the Reeve International Consortium on Spinal Cord Injury. Soon thereafter, however, he became ill with esophageal cancer (he died in 1996). Mary Bunge took his place in the Consortium. “It has been a remarkable and beneficial and exciting opportunity for me for which I am extremely grateful.” Dr. Bunge says the collaborative approach of the Consortium is essential. “Because we’re dealing with such a complex problem, we have to think of combination strategies. I don’t think any one of us is adept at all the techniques that need to be used to solve this very complex problem. I have a number of papers with other members of the Consortium. It’s been wonderful.”

— Sam Maddox
injury and paralysis than previously thought – the problem is much larger than any of us knew. Five times bigger than what was commonly stated. Our approach to the community is very straightforward, very honest, very true to what we’re trying to accomplish in terms of tomorrow’s cures and today’s care. We have an awful lot to offer. We have the Paralysis Resource Center, which is a major information asset. We have a robust quality of life program that provides grants to community organizations. We have research programs that span from basic discovery science to our clinical initiatives. I’m a big optimist in terms of where the Foundation is going. But there’s a lot of work left to do and we need the help of everybody who is touched by spinal cord injury and paralysis or knows others who are — and that’s virtually everyone.

Q: Your family has been involved with the Foundation since almost the beginning?
A: Yes, that’s right. Greg was injured around the same time Henry Stifel was, in 1982. His father, Hank Stifel, began the Stifel Paralysis Research Foundation the following year to support spinal cord research and it soon became aligned with the larger American Paralysis Association (APA). After Greg’s injury, we had started to look around for resources, to see who was doing research. But there was very little going on anywhere. Shortly after the Stifel/APA affiliation in 1986, my dad decided to commit to that organization. He volunteered quite a bit of time; his background was in finance and he helped institutionalize financial procedures and systems that were non-existent in those early days. APA was growing and building a solid base and over time we stayed involved in various aspects of the organization. Then Christopher Reeve was injured. He started his own foundation and then decided to merge with APA. At about that time, my family wanted to make a substantial gift to support SCI research. We thought about starting our own foundation. After considering that, and other organizations funding research, we decided to support the Reeve Foundation. The Foundation was already very substantial; they already had the infrastructure in place to vigorously pursue spinal cord injury research. They already had assembled a roster of the very best scientists to assure the integrity of the research program. They already had a fundraising structure. It made sense to support the Reeve effort rather than create something new. In terms of the choices my family made to invest both our time and money, I couldn’t be happier with where we ended up.

Q: You joined the board then, were you coming on as a finance guy too?
A: No, I had a particular interest in the research side. I joined what was then called the RPC, the Research Planning Committee. I’m not a scientist, I’m a layman, but the board decided that they wanted someone outside the research community who had some knowledge of the particulars but wasn’t necessarily a scientist — so that there would be some oversight. The committee did quite a bit of work in structuring how research is done, along with Susan Howley, who had attracted a really strong roster of scientific institutions and individual scientists to this area of research.

Q: You must on occasion get a phone call, maybe from a person who has a family member with a new injury. What’s your message?
A: What I tell them is that the spinal cord field now versus five or ten years ago is alive with exciting research and promise and that there is legitimate progress being made. It’s a completely different story going forward.
Q. What are some of the ideas you have as a board chair that can encourage the public to see the Reeve Foundation as a place to invest their charitable contributions?

A: We very much view ourselves as part of the large community of people affected by spinal cord injury paralysis, including friends, relatives, caregivers, doctors and scientists. That community needs to be involved in helping to move both research and quality of life initiatives forward to improve the lives of people living with paralysis. And obviously that takes money, so we want to be able to open up the avenues for participation as wide as possible. We want to attract donors from all segments of the community. We’re adding chapters and Team Reeve is expanding around the country. We have a formal affiliation with Life Rolls On. We have a very active presence on the Internet to encourage giving.

Q: Is there a strategy to build relationships among other organizations to spur progress?

A: Very much so. We have begun partnerships with organizations that raise funds for SCI research, including the Sam Schmidt Paralysis Foundation and the Quad Foundation. Also, we have an initiative on aging with paralysis that includes participation from the Kessler Foundation, the Miami Project to Cure Paralysis and the Craig H. Neilsen Foundation. Aging with a disability is emerging as an enormous issue for the field and for society at large. So it makes all the sense in the world that we work together on it. We all bring our particular strengths to different aspects of the problem, so to be able to collaborate with folks and bring a broader set of strengths to bear is good for everybody.

Q: People sometimes say, Reeve, you’re the stem cell people. Do you hear that as well?

A: We’re aware of it but people are getting a sense that the Foundation is about a whole lot more than stem cells. That doesn’t mean stem cells don’t have a role. The message that we would like to convey is that we are all about building this community and moving this field forward and not about one particular approach. I learned a long time ago that trying to tie yourself to one particular approach isn’t going to work, there’s no magic bullet for repairing the injured spinal cord. Even when you start to have therapies that have an effect on the physiology, you’re still going to have a whole host of other things that you have to deal with — bone density, bladder, strengthening muscles. How do you rehabilitate people? How do you do all of those things? There are huge areas of research that have yet to be undertaken. So it’s not as simple as stem cells curing everybody. And I think people are starting to realize that. The spinal cord is just enormously complex, and traumatic injury is not a static process. Patients eventually will be given a carefully orchestrated series of treatments and drug cocktails pegged to their type of injury, its location, time since trauma, their age, general health and so on. Then the question of what kind of rehab and how much looms large – it’s uncharted territory at the moment.

Q: Over the time Christopher Reeve was injured you met him many times. Do you have any insights about what drove him?

A: Chris was just a very special individual. He was determined not to quit and he never did. He wasn’t going to let paralysis define his life; it didn’t. He wanted to contribute and to be productive and he was — extremely so. What made him tick? He was just a very determined individual. The Reeve Foundation today is a big reflection of that determination. I think that’s what he left us, the idea that even when faced with great obstacles you keep going, you just do what you can to change it.

THE MICHAEL A. HUGHES SOCIETY is a community of planned giving donors – people who have generously included the Reeve Foundation in their estate plans. Planned gifts include bequests through donors’ wills, charitable trusts, and other life-income vehicles, and gifts such as retirement plans and life insurance policies. The Society is named for Mike Hughes, who came to the Reeve Foundation more than 20 years ago when his son Greg was paralyzed in an accident. Mike went on to become one of the Foundation’s most enthusiastic and hands-on supporters, providing wise counsel, encouragement, and, ultimately, an extraordinary gift. Two of his children are following in his footsteps, holding Reeve Foundation volunteer leadership positions. For more information about including the Reeve Foundation in your estate plans or making an outright gift, please contact the Development office at (973) 379-2690 ext. 7131.
Lorne M. Mendell, Ph.D., heads a laboratory at the State University of New York in Stony Brook. The Mendell lab, one of six in the Reeve Foundation International Research Consortium on Spinal Cord Injury, is focused mainly on plasticity of the mammalian spinal cord – that is, the ability of nerve cells to adapt after trauma or disease. The specialty in this lab is electrophysiology, a field of research that measures the electrical activity of nerve cells. This is valuable for understanding the process of recovery and the effects of various treatments on nerve cells, especially when the effects are not obvious in the behavior of the animal.

The Consortium, by design, encourages collaboration between labs. Indeed, that is how Dr. Mendell’s current work has emerged. The Consortium labs of Reggie Edgerton, Ph.D., at UCLA and Rusty Gage, Ph.D., at The Salk Institute have been integral to Mendell’s most recent efforts. Edgerton’s research underpins the idea that activity and rehabilitative training enhance recovery; this is why, for example, locomotor or treadmill training can improve outcomes for people with spinal cord injury. Coincidental to recovery of function, however, Edgerton’s team noted that production of certain neurotrophins or growth factors – NT-3 and BDNF – was increased after locomotor activity. Dr. Mendell’s lab had been studying the physiology of neurotrophins in the context of pain and synaptic plasticity. Meanwhile, Gage’s lab has developed genetic techniques to enhance levels of these growth factors in the spinal cord in vivo. Working with his postdoctoral fellow, Dr. Vanessa Boyce, Dr. Mendell combined those strategies and used his behavioral and electrophysiological techniques to better understand the effect of growth factors and of activity (or training) on neurons in the spinal cord.

“The fact is,” says Dr. Mendell, “the spinal cord below the level of an injury is alive; it works. It’s just disconnected from the brain. We can show videos of adult rats with fully transected spinal cords – the animals step or hop on a moving treadmill after treatment with neurotrophins. Of course the hind limbs are not coordinated with the forelimbs, and the rats require support in order to achieve balance. Our electrophysiological recordings from these same animals provide suggestions of possible mechanisms initiated by treatment with the neurotrophins that could account for the stepping. The question is, how do you activate these circuits reliably to support useful behavior? This is not a trivial problem and may require combination with other approaches. This is the value of the Consortium since we have a broad array of approaches with which to combine neurotrophin treatment; plans are underway to exploit this translational possibility.”

Several recent journal papers, in print or progress, also underscore the joint effort between labs to enhance neural function. “In this study,” says Dr. Mendell, holding a manuscript, “we combined our interest in NT-3 with our long-standing focus on NMDA receptors [key molecules for controlling plasticity of nerve synapses and memory]. We then became interested in combining them with anti-Nogo, which is studied in the Schwab laboratory [Consortium lab of Martin E. Schwab, Ph.D., at the University of Zurich, Switzerland] or with chondroitinase, which is studied in the Fawcett laboratory [Consortium lab of James W. Fawcett, Ph.D., University of Cambridge, Cambridge, UK].” Both of these studies were carried out with Dr. Victor Arvanian, a research scientist formerly in Dr. Mendell’s lab and now at the VA Medical Center in Northport, Long Island. The aim has been to encourage the formation of conducting detours around a partial injury of the spinal cord. Initial results are encouraging and we hope to be able to use these results, perhaps in combination with others, to improve function of the partially damaged spinal cord.

Dr. Mendell explains his specialty: “One of the things you learn when you do electrophysiology is that even though neurons might look perfectly normal in the microscope, they might not be functioning normally. That could mean you didn’t know what you were looking for when you did the anatomical studies; you didn’t have the right stain or you weren’t looking at the right parameter. Sometimes electrophysiology will bring that out for you, particularly if it involves the behavior of neurons under dynamic conditions.”

As an example, Dr. Mendell describes an experiment where electrophysiological recordings helped to open up a new understanding of the damage produced by spinal cord injury. “We had done hemisections of
the spinal cord which involve damaging only one side of the cord. We originally expected that there would be no difference in conduction of nerve signals on the other side of the spinal cord immediately across from the damaged side. But we were very surprised to find that there was a rather substantial change in conduction beginning after several weeks. Once you see that something has happened,” says Mendell, “then one can look for the cause. In this case, it may be that inflammation leads to changes on the uninjured side, perhaps by increased levels of molecules known as proteoglycans.” Taking the concept a step further, Dr. Mendell speculates that any treatment that could depress the level of proteoglycans might lead to recovery of conduction in the spinal cord. He is now recording electrical activity in the brain to identify any effects of chronic spinal lesions on sensory input to the brain.

Only recently have scientists begun to understand that spinal cord trauma affects the entire nervous system.

“Measuring behavior can be fraught with challenges,” says Dr. Mendell, “and sometimes it can be very difficult to really understand what changed. There might not be a big enough or coherent enough change to observe something in the behavior. Or the behavioral change may be too complex to determine where the change has occurred. So that’s where electrophysiology can be helpful — we can know with certainty that a particular pathway has changed. And if that is the case, then we can try to devise ways to strengthen the change so it will affect the behavioral outcome, which is after all, what we’re really interested in.”

Collaboration is more than a good idea; it’s really the only way most neuroscience studies get done now. Says Dr. Mendell, “The field is so big and the spinal cord is so complex that no one person or lab alone can expect to solve the big problems such as restoring function after spinal cord injury. You can certainly see this in the way papers are written. As a Ph.D. student, my thesis paper was authored with me as sole author. As a postdoc, the only authors on the papers were my postdoctoral advisor and me. The more usual thing today is a published paper with many more authors from two or more labs.”

Knowledge is more and more specialized and this dictates the need for collaboration. “Although present knowledge encourages us to believe that we can improve the lives of spinal injured people, we are still missing many important pieces of the puzzle. We need a steady stream of new ideas from basic science, as well as novel ways of translating them to achieve practical benefits for people with spinal cord injuries.”

Dr. Mendell sees science as an interactive dynamic process, an activity undertaken by a community of investigators. “The important pioneering findings generally will stimulate the experiments of others, and this is what brings them into the scientific mainstream. They will be discussed by the community and their reproducibility will be determined on the way to building on them to obtain subsequent results. So science today is not what I originally thought it was when I began as a young student: that it was sort of a solitary endeavor, the concept of the ivory tower. It’s not that at all. It’s very social. It’s a lot different from what it was like when I began in science.”

— Sam Maddox
ANIMAL CORE LAB: BUILDING RESEARCH CAPACITY

The International Research Consortium on Spinal Cord Injury is a Reeve Foundation initiative to build collaboration between a group of distinct laboratories. The idea is to focus the brainpower of top scientists to more quickly exploit the capacity of the adult nervous system to repair and remodel itself and to switch on nerve regeneration after injury.

Aside from the basic research of the group’s principal scientists, the Consortium also features a common lab that performs specialized work for member labs, for investigators in the SCI field outside of the Consortium, and even for the biomedical industry. Aileen Anderson, Ph.D., is scientific director of the Consortium’s Animal Core Laboratory at the University of California, Irvine. She explains what the Core lab does.

“At the time the Consortium was formed, only a handful of the labs had direct expertise in spinal cord injury. The rest of the players were SCI novices—well respected within their individual fields, very prominent labs, but from other research areas.” The array of Consortium labs had specialization in Alzheimer’s studies, stem cells, electrophysiology, developmental biology and gene transfer. “The goal,” says Anderson, “was to get the various labs to direct their particular expertise to the problem of spinal cord injury.”

Forming a focused collaborative network meant that the labs had to either quickly develop expertise, or rely on the labs teaching those skills. Says Anderson, “If any of the Consortium labs wants to run a spinal cord injury experiment, we can assist with the experimental design and indeed run the full project for them right here. Typically, our role involves the animal model and surgical components, but it can involve everything through histology and returning data at the end of a full study.”

The Core is often used as a training facility. “If Consortium lab postdocs need training in any sort of technique, say in behavioral assessment, or anesthesia, or in any number of technical things their home labs are not well versed in, they can come here to the Core for training.” There are no fees or costs to the Consortium labs.

The role of the Core has expanded over time to include contract lab work and training for scientists who are not in the Consortium. Says Anderson, “Basically an individual investigator, once approved by our Consortium Advisory Panel, is granted access to the Core. They don’t pay anything. They may supply us their compound, their cells or whatever it is and we’ll run the experiments. They can come in and get training, very much like a Consortium member would, or they can come here and work with us to run a full project.”

The idea is to give people who may not be SCI experts a chance to get some pilot data. “They may be immunologists or tissue engineers who have a compound or a drug or a scaffold or cell that has a potential application in the spinal cord injury; and by working with us, they can gather enough data to know whether they take that next step and apply for actual funding through the Reeve Foundation, the NIH or other resources. We’ve worked with a lot of different investigators who have been successful turning their Core pilot data into research grants.”

The Core also services the biomedical research industry. “The Reeve Foundation is interested in expanding opportunity and ideas toward its mission to develop treatments for SCI. As an example, maybe a biotech company has a compound for multiple sclerosis and wants to know the potential application for spinal cord injury. To organize a rigorous experiment for testing the compound in a spinal cord injury model is an enormous hurdle for most companies, but we, basically, can grant them access into the Core.” Companies pay for chemicals, reagents and basic costs. But they don’t have to pay anything for personnel or expertise.

“We can run a full project for them to give them preliminary data back—a thumbs up/thumbs down to give validation to their idea, to see whether it shows promise and should be pursued. The Reeve Foundation hopes, therefore, to stimulate industry and perhaps bring new treatments bench-to-bedside a little bit quicker. Access to our Core might broaden the horizon for an existing drug that biotech otherwise wouldn’t have considered for SCI. They might find an approach here they otherwise would not have discovered.”

There are no contract labs in the US that can run spinal cord injury experiments. “Biotech companies rely a lot on contract labs. If you want to do stroke work, you can send compounds out to Charles River for testing. If you want to study diabetes, you can send compounds...
out to a number of contract labs and get a preliminary test. If you want to test your materials for spinal cord injury, our Core lab makes it possible.”

The Core staff varies between four and six technicians. It is managed by Rebecca Nishi. “Rebecca is phenomenal; she interfaces with some of the Consortium or individual investigators directly and, mercifully, does most of the nitty-gritty tasking, record keeping and problem solving.” There is endless detail to track. “Every project, every surgery sheet for every animal, every behavioral assessment sheet, every data analysis file for every animal injury, every immunostaining record sheet, all of that gets tracked and coordinated and put together very much as if we were doing good laboratory practice at a biotech company for FDA submission.”

Anderson says staff have to be versatile, and broadly trained. “They might spend one week doing nothing but surgeries. That can be a four-to-six-person job for seven days straight. The next week, they might do nothing but sectioning and immunostaining. To get a technician fully trained and up-to-speed takes at least six months, actually closer to a year – we need them to perform at a very high level.”

Anderson also has her own workload at UCI. “I direct the Core but I also have a lab with 20 people in it working on two different aspects of spinal cord injury: the role of inflammation in SCI and the effect of transplanting human neural stem cells and human embryonic stem cells that might be used to effect repair and recovery.

Because Anderson’s lab at UCI works with stem cells and spinal cord injury, she attracted attention for research showing therapeutic effect in animal models. “I get calls from Newsweek and Science and certainly from patients. The number of patient inquiries that emerge after every stem cell paper that has to do with spinal cord injury is staggering. And all of us who do SCI research hear this question: ‘My brother was just injured this morning in a car accident and they’re telling me he’s C3 and he’s never going to walk again. Can we fly him to China to get a stem cell transplant?’ The big message I try to convey is simple: There are studies that have looked at people who went overseas for stem cell transplantation. Those studies have shown no beneficial effects but they have shown adverse events in certain cases. And so despite what you might find on somebody’s blog on the web, the clinical data don’t support the idea that this transplant is going to be a good thing for you. I tell people there are published reports of those kinds of transplantations resulting in tumors and making people worse.

“I emphasize that there are cell therapies that are going to clinical trial now that might be beneficial and that a transplant in China now will make a person ineligible for any future therapies shown to be safe and effective. Sadly, a lot of people don’t want to hear that.

“The other thing I feel quite strongly about is the locomotor treadmill training data. Stem cells aren’t there yet but locomotor training is. I’ll direct them to the Reeve Foundation’s NeuroRecovery Network. I encourage them to consider doing very intensive step training rehab – it’s what I would personally do if I were injured or if it were my daughter, family member or friend. I stress that I would not go to China – or any other off-shore clinic offering cell transplants.”

– Sam Maddox
NEW INDIVIDUAL RESEARCH GRANTS

Concomitant Function: Investigation of mechanisms of transcranial direct current stimulation of motor cortex for treatment of chronic pain in spinal cord injury
Felipe Fregni, MD, PhD, Spaulding Rehabilitation Hospital, Boston, MA

Chronic pain is a serious consequence of spinal cord injury (SCI) and has a significant impact on quality of life. No satisfactory treatments are available. Dr. Fregni, a neurologist also affiliated with Harvard Medical School, believes that chronic pain results from poor sensory processing in the brain after the loss of input from peripheral sensory systems due to spinal cord injury. Because drugs have a diffuse effect they offer limited benefits for pain control. He suggests a more focal attack.

Until recently the only method to modulate pain-processing centers was with the use of invasive brain stimulation – with electrode placement using neurosurgical techniques. This method is costly and associated with surgical risks, but Dr. Fregni’s team has shown that a new non-invasive, relatively simple method of brain stimulation – transcranial direct current stimulation (tDCS) – reduces pain in spinal cord injury. In an earlier study, there was “remarkable” pain reduction in patients with untreated chronic spinal cord injury pain. He now proposes to assess the mechanisms of action of tDCS in alleviating pain using the state-of-art methods such as magnetic resonance spectroscopy, single and paired pulse transcranial magnetic stimulation (to assess cortical excitability) and electroencephalogram. It is hoped the results of this study will speed the development of this novel therapeutic approach and will also shed light on the causes of chronic pain in spinal cord injury.

Felipe Fregni

Neuroprotection: The impact of age on inflammation, neural apoptosis and axonal survival after spinal cord injury
Julio Cesar Furlan, MD PhD, The Toronto Western Hospital Research Institute, Toronto, ON

Aging of the North American population has considerably increased the proportion of those over 65 with spinal cord injury from 5 percent in 1973 to 18 percent in 2003. Dr. Furlan’s recent work has shown that while the mortality rates in the elderly with SCI are dramatically higher than in the younger population, elderly survivors do indeed have the potential for good functional recovery.

This raises important questions: (a) what pathobiological factors in the elderly contribute to increased mortality after SCI? (b) are there mechanisms that can be modified to improve outcomes in the elderly with SCI?

Furlan’s team hypothesizes that an altered inflammatory response in the elderly with SCI contributes to adverse outcome. He plans to investigate this hypothesis by studying immunoochemical, neuroanatomical and molecular investigations in spinal cord specimens donated for research purposes. The project will compare the number of inflammatory cells and neural survival within spinal cord sections from both elderly and younger individuals and examine programmed cell death (apoptosis) of oligodendrocytes in the spinal cords of injured and uninjured individuals from older and younger patients. Furlan hopes the research project will lead to therapies to limit inflammation and protect nerves, and to cell-based treatments individualized according to the age group to optimize outcome after SCI.

Julio Cesar Furlan

Concomitant Function:Effects of Respiratory Muscle Training and Functional Electrical Stimulation on Task Specific Respiratory Muscle Activity in Individuals after Spinal Cord Injury
Alexander V. Ovechkin, MD, PhD, University of Louisville, Louisville, KY

People with upper thoracic and cervical injuries often have pulmonary complications associated with respiratory muscle weakness, paralysis and spasticity. Lack of muscle strength and poor respiratory muscle control lead to breathing insufficiency and ineffective coughing; this can lead to airway obstruction and the development of pneumonia. Inspiratory muscle training with resistive loading is known to increase inspiratory muscle strength and endurance, leading to improved pulmonary function. However, little is known about the effectiveness of expiratory muscle training in SCI patients. Dr. Ovechkin and his team suggest that resistive cycle inspiratory and expiratory muscle training...
(RMT) in combination with functional electrical stimulation (FES) for expiratory muscles will improve pulmonary function by facilitating spinal neural networks for breathing and by restoring respiratory muscle activity. They predict that RMT synchronized with FES will significantly increase respiratory muscle strength and endurance, thus improving the breathing function of individuals with chronic cervical SCI with intact phrenic innervation.

This study will recruit 24 people with cervical SCI with intact phrenic nerve and 10 neurologically intact individuals (to evaluate normal baseline variables). Ovechkin will assess respiratory muscle control, pulmonary function and respiratory functional outcomes using surface electromyography (sEMG), spirometry, respiratory muscle strength (RMS), respiratory muscle endurance (RME), and peak oxygen consumption (VO2 peak) tests. Testing will be performed before and after the RMT or FES and after a three-month follow-up period.
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