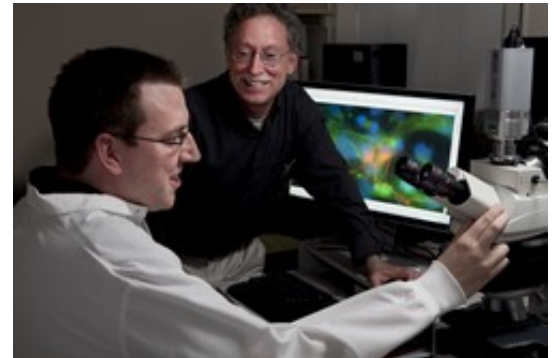




## Thirty Years Ahead of the Curve: The Center for Spinal Cord Research

Approximately 250,000 people in the United States, mostly young men, suffer from spinal cord injury (SCI) with 10,000 new cases added every year. According to a recent study from the Christopher and Dana Reeve Foundation, the actual number of people with spinal cord injury is much larger, estimated to be 1,275,000 with a total annual cost of roughly \$40.5 billion.



To date, SCI research and advances in therapy have come from private foundations, the government, and academia. The historic dearth of research and clinical application is why the work being conducted by the Spinal Cord Research Center at the College of Medicine is so vital: 450,000 people, and their families, depend on these scientists to find viable alternatives and improve their quality of life.

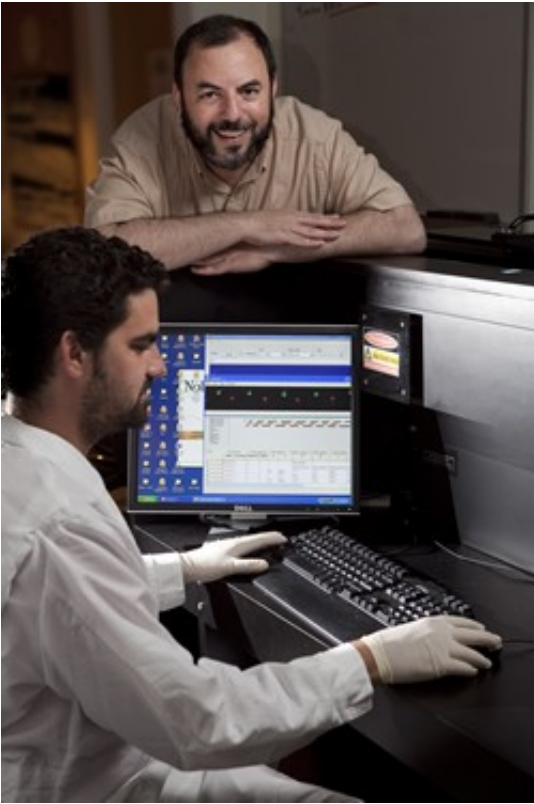
Until quite recently, popular belief held that there was no rehabilitative hope for those with SCI because the spinal cord will not regenerate. "Treatment" was merely physical stabilization. Actor Christopher Reeve's highly publicized 1995 spinal cord injury brought national attention, and then the financial support of his eponymous foundation, to the desperate need for research in the field. Although the Spinal Cord Research Center has been conducting this important work for over 30 years, the pace of discovery has accelerated since the late '90s.

The Center, founded at the Medical College of Pennsylvania, has evolved into a nationally recognized, multi-institution endeavor. Since the mechanics of spinal cord injury are so complex, research into its remediation is similarly multi-layered and must be addressed from a variety of approaches. The Spinal Cord Research Center prioritizes this combination approach to investigation.

Itzhak Fischer, Ph.D., chair of the Department of Neurobiology and Anatomy at the College, states that SCI research must be concerned with both anatomical aspects and behavioral aspects of the trauma, particularly because spinal cord injury occurs in two waves. First, there is the initial physical injury, typically resulting in a variable degree of paralysis. Then, the secondary injury stems from inflammation, expansion in size of the original injury site, and onset of neuropathic pain.

Professor John Houle, Ph.D., Spinal Cord Research Center director, comments, "Secondary degeneration can occur over weeks to months.... We can't do anything about the primary [injury], but it's the secondary that we're trying to control and not allow things to get worse than they are."

In order to do this, the Center has developed a combination of therapies and engages a number of diverse departmental experts. Both Dr. Fischer and Dr. Houle observe that some of



the research is so cutting edge, it seems as if it could be science fiction a decade or two ago. Yet, testing of procedures to affect neuroprotection, neuroregeneration, and rehabilitation of the spinal cord are always at the forefront of the research. "Because [SCI] is so complicated, because there are different events at different times, there isn't a simple approach," Dr. Fischer insists. "There isn't a drug or type of cell therapy that is going to solve all of it." At the Center, scientists investigate ways to reduce the secondary injury (pain and inflammation), repair and regenerate the damaged spinal cord (through the use of transplants and growth factors), and rehabilitate or retrain the spinal cord adjacent to the level of injury.

Dr. Houle elaborates on this process. Immediately after injury, they administer a drug as a neuroprotective measure. Then, after a few months, they "...do a neuroregeneration approach, usually transplantation of a peripheral nerve.... We'll take a [peripheral] nerve out of the leg and graft it to the spinal cord. This will allow nerve fibers in the spinal cord to regenerate.... But we have to try to get them past any of the dense scar tissue present at the lesion site." This is followed by rehabilitation. "It's not just physical exercise, but it's really trying to train the nervous system to begin working in rhythmic fashion," attests Dr. Houle. "There are good indications that we have some level of functional recovery when we combine all of these procedures."

A device called the "catwalk for rats" is used to detect this possibility of functional recovery by rehabilitation. Rats with SCI enter a small chamber, and optical sensors detect and measure the profile and strength of the animal's steps. Dr. Fischer emphasizes that it is critical to discern the difference between muscle function and spinal cord function. He says, "The new approach that we use here is to try to train the spinal cord to work more efficiently with what is preserved in the spinal cord itself, to become more adaptable for locomotion after the injury."

At the same time, other scientists examine pharmacological methods and computer and robotic models of recovery. The neuroengineering group, for example, seeks to "...generate sophisticated prostheses that will be connected to the brain – forming a brain-machine interface.... [They are] trying to circumvent the deficiency of spinal cord injury, not to repair the spinal cord, but to get those signals from the brain around [the damaged site]," says Dr. Fischer. "We have a collection of investigators that are coming from a behavior and activity background, from stem cell biology, from pharmacology and bioengineering." As Dr. Houle affirms, "It helps having people look at [SCI therapy] from many different perspectives."

The Center's unique combination approach necessitates a multitude of specialized labs in which to conduct the clinical tests. The various facilities make it possible to investigate the "different models of injury" in a "quantitative way." As Dr. Fischer explains, "A single lab cannot afford all the expertise in terms of surgical facilities, outcome measures, imaging, anatomy.... At the end of the day, we need to test a lot of approaches...." He says there may be only four or five centers in the United States that have this capability.

Since its inception in the mid-'70s, one of the Center's enduring strengths has been its reliance on collaboration, not just among multiple academic disciplines, but with other schools, hospitals, and institutions as well. The Center enjoys a strong working relationship with Allegheny General Hospital and the Shriners Hospital for Children in Philadelphia. In the case of

Shriners (whose Philadelphia branch is known for its pediatric spinal cord expertise), there is an open dialogue concerning patient needs and how the Center might use clinical models to address those needs.

Currently, the Center is the only NIH-funded spinal cord research program in the country. Despite this highly prestigious million-dollar project program from the NIH, funding is an ongoing challenge. The Center is one of the few such organizations in the nation without an endowment. In the face of uncertain financial support, the Center remains focused on its mission: to develop therapeutic strategies that promote the recovery of function lost after spinal cord injury. For those affected, this research is often a matter of life and death.

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