

Everything we knew about rehab and research is being turned on its head. Rehab is no longer a once-and-done deal — function can be improved upon, and people are already healing from spinal cord injury. Are we talking cure? No. But we are talking about regaining abilities.

1. Disregard SCI Dogma

INTERVIEW WITH WISE YOUNG BY SETH MCBRIDE

NEW MOBILITY: When we contacted you for this story, you sent an email about why the dogmas of SCI research are slow to die. Can you explain these dogmas?

Wise Young: The first and most influential dogma is the belief that the spinal cord does not regenerate. Hundreds of published studies have shown that the spinal cord not only can, but does regenerate. In fact, the more severe the injury, the more regeneration occurs.

The second and sister dogma is that people do not recover from spinal cord injury. This is false. People with incomplete injuries usually recover substantially and even people with complete injuries will recover partial function.

NM: If the spinal cord is able to regenerate, what has been holding people with spinal cord injuries back from recovering function?

WY: We did a study in China [published in 2016] using umbilical cord blood mononuclear cell transplants combined with an intensive locomotor training program — six hours a day, six days a week for six months. That study showed that 15 out of 20 people with complete SCI recovered long distance walking, as well as bowel and bladder function by one year after the start of treatment. In that trial, there were eight who received the UCBMNC transplants but no locomotor training. They did



If SCI research has a father it's Dr. Wise Young. From his 1990 discovery of high-dose methylprednisolone as a treatment for SCI to the scores of clinics he has built globally, to his current discoveries of what happens when stem cell treatment is combined with exercise, he has always been on the cutting edge of SCI research.

not recover walking, bowel or bladder function. This was like a control group of sorts. The message was clear — no exercise, no recovery.

We did another study that should be published soon, which involved 30 subjects. All received the same intensive locomotor training, and half received a surgery to remove all adhesions, clean the spinal cord and surrounding membranes. This is called untethering. None received any cell transplants. About a quarter of them recovered walking, but a majority showed improved bowel and bladder function. The two treatment groups showed no difference in walking, but the untethered group had better bowel and bladder recovery. I think that trial showed us that walking by itself is beneficial. *(For more on untethering and Dr. Young's research, don't miss NM's October cover story.)*

If we think about it, these findings are really not so surprising. Animal studies have shown for a long time that spontaneous regeneration occurs in the spinal cord and that transplanted cells can improve the regeneration, but the regenerated axons are very unlikely to make exactly the same connections. Training is necessary for the brain to learn to interpret sensory signals and how to use the new connections.

FUNCTION



Clinicians and researchers at the Shirley Ryan AbilityLab in Chicago are working together in groundbreaking new ways that could transform the future of acute rehab (see sidebar, page 44).

NM: Were there any other notable findings from these recent studies?

WY: One aspect of the studies was really unexpected — age and time after injury did not seem to make a difference. People that were in their 50s and 20 years after injury recovered as much and as well as those who were in their 20s and two years after injury. If you had asked me before the study whether age or time after injury would affect regeneration and recovery, I would have responded that both would be important. This finding suggests strongly that the spinal cord is ready to regenerate and to recover function even 20 years after injury and in older patients.

NM: For decades, SCI recovery had been framed in terms of a “cure,” as if recovery was going to come in the form of a pill or a surgery that suddenly restored full function to a paralyzed body. What is a more accurate way to view restoration of function?

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WY: The spinal cord injury community has been really disheartened by the continual barrage of media reports that the cure for spinal cord injury is here, only to find out that it won't be available for another five years — they called this “the rolling fives.” Although we've published these studies, we made the choice not to publicize them, instead explaining the results with individuals and groups within the SCI community. We need to explain how this recovery works so that people don't misunderstand that it's not a cure. We're not talking about miracles here. Recovery in spinal cord injury can be helped by certain therapies and requires a huge commitment on the part of the people with SCI and their families to do the locomotor exercise, which is the most intensive exercise they'll ever have. To take somebody who's 20 years after spinal cord injury and expect them to walk without intensive training, that's expecting a miracle to happen.

NM: Where does your research go from here?

WY: We're trying to get worldwide regulatory approval. We have a trial that will be starting in the U.S. within the next six months that has already been approved by the FDA as a phase 2 clinical trial. This will be the first trial in the U.S. using umbilical cord blood cells transplanted into the spinal cord, and this is the most intensive walking training program ever, and we have to show that it's feasible, that it can be done.

Phase 2 trials are preliminary to establish the feasibility, optimal dose and optimal outcomes for phase 3 trials. Generally, one does phase 2 trials until one is pretty certain that the phase 3 trial will succeed. Then we would go ahead with the global phase 3, which is the pivotal trial that forms the basis for regulatory approval.

NM: You've said that getting regulatory approval may be the only way for people to start thinking beyond the dogmas

and accept that regeneration and recovery are possible. If things go well, and you're able to get approval, how does that change the SCI research and clinical world moving forward?

WY: Big Pharma will take an interest. Right now they have no interest, they don't believe this can happen. Even after we published our study in 2016, there have been three clinical trials in the United States involving cell transplants into the spinal cord, and none of these three studies have employed intensive training. These three U.S. trials involved a number of different cells, and all resulted in no recovery of function. I don't know that their cells didn't work. All I know is that if they put in cells without walking the subjects, they're not going to see improvements in walking.

NM: Would you expect that if researchers start to include locomotor training or other activity-based training into their studies, then all of a sudden, we're going to start seeing a lot more successful studies for regeneration?

WY: Absolutely. I believe that. I don't think that umbilical cord blood mononuclear cells are the be all and end all of spinal cord injury transplant therapies. A lot of different therapies are showing some beneficial effects. There have been more than a hundred studies published in China in the last four years using transplants of a variety of cells into the spinal cord, and in every study, you notice that maybe two or three or four people are actually recovering well, and these are the ones who are highly motivated to walk.

It is a very exciting time in spinal cord injury research and for the spinal cord injury community. I suspect that what we have found in spinal cord injury applies to many other neurological conditions, including traumatic brain injury and stroke.

RESEARCHERS AND CLINICIANS JOIN FORCES

In 2017, the Rehabilitation Institute of Chicago — long recognized as one of the best neurological rehab centers in the world — opened a new headquarters and changed its name to the Shirley Ryan AbilityLab. Along with the new building and new name, the facility launched a whole new model of operating, becoming the first-ever “translational” research hospital where researchers and clinicians would work alongside one another. “We knew going in that 86% of scientific discoveries never make it out of the lab,” says Megan Washburn, the director of communications for AbilityLab. “In a typical setting, research is on a different floor or it's across the street or down the road. In our hospital they're smack dab in the middle of where clinical care and therapy takes place.”

The idea is to let researchers see first-hand the challenges of SCI rehab, let that experience inform their research and then collaborate with clinicians and patients to translate research into effective therapeutic interventions. Spinal cord injury applicable trials include everything from neuromodulation — using transcranial magnetic stimulation combined with electrical muscular stimulation and physical therapy to improve voluntary muscular function — to intermittent hypoxia research — a novel approach where brief periods of low oxygen have been found to increase the connection strength between brain and spinal cord for a few hours, giving a window to make therapy sessions more effective.

Washburn says there's already been interest in the translational model from organizations around the world. If more facilities start using the approach, we may see the next generation of big ideas quickly turn into real-world solutions.



The equipment at the Shirley Ryan AbilityLab is state-of-the-art.