CHRISTOPHER & DANA REEVE FOUNDATION
TODAY'S CARE. TOMORROW'S CURE.

[THE BIG IDEA]

REEVE FOUNDATION "THE BIG IDEA" FAQs

What is The Big Idea?
The Big Idea is a clinical research project to test the hypothesis that epidural stimulation can be used to promote significant improvement of cardiovascular, respiratory, bladder, bowel and sexual function in spinal cord injury patients who have been diagnosed as completely paralyzed. We have the opportunity to change the lives of individuals who were told nothing could be done for them. The research team believes The Big Idea study can foster a series of 'cures' that will improve the autonomic functions lost with spinal cord injury, including bladder, bowel and sexual function; temperature regulation; and cardiovascular function. These 'cures' – plural – are victories over paralysis. For the first time, there will be a treatment to ameliorate some of the health- and life-threatening consequences of spinal cord injury (SCI).

Who is leading The Big Idea?
The Christopher & Dana Reeve Foundation, together with prominent neuroscientist Susan Harkema, Ph.D. (University of Louisville) members of the NeuroRecovery Network® (NRN) and North American Clinical Trials Network (NACTN); key stakeholders and leaders from the spinal cord community; select Reeve Foundation board members; and Reeve Foundation staff members. For more information on The Big Idea, visit www.reevebigidea.org.

What are we raising money for?
We want to test what we believe is one of the most promising potential therapies for individuals living with spinal cord injury. The Big Idea is a $15 million campaign to fund a research study of epidural stimulation in 36 patients.

What are the goals of The Big Idea?

1. Raise the $15 million needed to support the campaign.
2. Test the hypothesis that epidural stimulation can be used to promote recovery of autonomic control in patients who have been diagnosed as completely paralyzed.
3. Ultimately, provide a safe and effective treatment for patients living with spinal cord injury that has the potential to improve their long-term health and quality of life.

When and how did the Big Idea campaign begin?
Over the last three years, Dr. Reggie Edgerton (UCLA) and Dr. Susan Harkema (University of Louisville) have implanted an epidural stimulation system in four "motor complete" spinal cord injured participants. The goal of this experiment was to assess whether a combination of epidural stimulation of the lower spinal cord and intense Locomotor Training could enable standing and walking. Although the experiment did not achieve the stepping goal as originally hoped, the ability to bear weight and recover voluntary movements in the legs, hips, knees, ankles and toes were easily achieved early on in all four participants. (The lack of success in enabling walking was believed to result from the limitations of the implantable system – an off-the-shelf stimulator used for pain control – rather than the hypothesis itself.) The ability to stand, however, was sufficient to prove the concept that there is memory inherent in the nerve networks of the spinal cord that can respond to sensory stimulation.

Indeed, the stimulation allowed the patients to voluntarily control some movement of their lower extremities. Most remarkable and unexpected, however, was the improvement all four patients experienced in the functioning of their autonomic nervous system. Each saw a dramatic improvement in bladder, bowel and sexual function, regulation of body temperature, and cardiovascular health.

This recovery suggests that there remains some residual connection between the brain and the spinal cord that was undetectable post-injury; we are just seeing the "tip of the iceberg" regarding the potential for epidural stimulation. Although the development of more sophisticated implantable systems to enable walking is underway, the Reeve Foundation feels a moral imperative, in light of these first four participants, to explore the quality-of-life benefits with epidural stimulation in a broader range of patients.

What is epidural spinal cord stimulation?

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Epidural stimulation is the application of a continuous electrical current, at varying frequencies and intensities, to specific locations on the lower part of the spinal cord. It involves an implanted microarray over the dura of the lumbar cord. It is believed that epidural stimulation reawakens the nerve networks in the spinal cord. *Note: epidural stimulation is not the same as functional electrical stimulation, commonly used to activate paralyzed muscle by direct application of an electrical charge. Epidural stimulation does not activate muscle; it activates nerve networks.*

Why is the Reeve Foundation so excited about epidural stimulation?
Although individuals living with SCI can be expected to live near-normal lifespans, most struggle with a host of debilitating and life-threatening health dysfunctions. These can include poor cardiovascular and respiratory function, loss of bladder, bowel and sexual function, skin breakdowns, loss of muscle mass, body temperature and blood pressure irregularities. At the present time, there are no effective treatments for these conditions other than standard medical care.

Epidural stimulation may change this by effectively and safely improving the function of a person's autonomic system, which oftentimes is badly compromised as a result of injury. It is possible that epidural stimulation might be combined with other interventions to promote a more robust and/or complete recovery.

Positive results in this 36-participant study would be compelling justification for translating the intervention into the clinic so it can be made available to the many individuals living with paralysis who could benefit from it. Our hope is that this treatment will also be effective in paralysis caused by other neuromuscular disorders such as stroke and Parkinson's, thereby broadening the patient population benefitting from its use.

What happens to these patients after the study ends?
Study subjects will make an approximate three-year commitment to the research after which they will be given the option to keep or remove the stimulator. (They may also opt-out at the conclusion of the first year.) They will have long-term follow-up after the initial three-year commitment: clinic visits every six months until the device is either removed or approved by the FDA for this particular use.

Lastly, if any findings emerge during the study which are beneficial to the subjects, the investigators will seek IRB and FDA permission to allow them to "practice" the stimulator therapy at home.

When will this be available to more patients?
Positive results in this study would be compelling justification to work with the appropriate medical, regulatory and health insurance authorities to move the treatment into broad clinical application; the timeframe for this has not been determined. Our mission with The Big Idea is to bring epidural stimulation to the clinic as quickly as possible. However, the first step is to replicate the study with an additional 36 participants, collect safety and efficacy data on the implanted subjects, open lines of communication with regulatory agencies and understand the best pathway to move epidural stimulation into the clinic.

How do I qualify as a subject for this research?
Subjects must meet the inclusion/exclusion criteria as defined in the research protocol. Additionally, the Reeve Foundation, working closely with the Principal Investigator, has developed a patient selection process which will govern how all potential study subjects are chosen. The University of Louisville manages a patient registry for all clinical research programs being conducted there, including epidural stimulation. To learn more and apply as a potential candidate for future spinal cord research please visit: http://louisville.edu/medschool/neurosurgery/harkema/form/

What differentiates this project from other research projects you fund?
The epidural stimulation clinical project is a logical extension of several decades of discovery science funded by the Reeve Foundation. This basic science underpins much of today's fundamental knowledge about how the normal spinal cord functions and what happens during the injury continuum, from the point of trauma through the biological cascade of secondary damage and cell death. Discovery science also helped scientists begin to understand how activity-based exercise – such as Locomotor Training - could enhance the body's own repair process. Now, building on that fundamental knowledge, the Reeve Foundation is expanding its basic science programs to include this clinical research study in the hope of identifying a new and effective treatment for some of the consequences of spinal cord injury.

The Reeve Foundation, which has provided more than $110 million in research grants to hundreds of scientists around the world, continues to maintain a robust research portfolio. Our funds have nurtured new talent and ideas and facilitated unprecedented scientific collaboration and communication. Other current Reeve Foundation research programs include the International Research Consortium on Spinal Cord Injury; NeuroRecovery Network® (NRN); and North American Clinical Trials Network (NACTN).

Reeve-funded research continues to be focused on many exciting lines of science: cell replacement (including stem cells), nerve growth promotion and guidance, axon bridging, immune system modification, neuroprotection, and neurosprosthetics.

What is the timeline for the research project?
Our hope is to begin the clinical study in early 2015; it is expected to take five years from start to finish.

How long will the campaign last?
The campaign began June 1, 2013. We want to raise $15 million by spring 2015.

Where can I find out more information about The Big Idea and epidural stimulation research?
A wealth of information and resources about The Big Idea can be found on the campaign website: www.reevebigidea.org. This site also captures donations and will be updated periodically to reflect new information and content.

How can I help?
We need to raise about $3 for every single American with paralysis - 5.6 million people – to raise the funds necessary - $15 million - to make this research project happen. The Big Idea represents an opportunity for your contribution to make a difference for thousands of people in the here and now.

How long do I have to fulfill my pledge?
Pledges must be fulfilled by December 31, 2015.

How do I make a gift or pledge to the Campaign?
Your commitment of support makes a needed difference. To make your Campaign gift or pledge today, please contact Aimee B. Hunnewell, Reeve Foundation Senior Vice President of Development, at (973) 379-2690 x7131 or *Aimeeh@ChristopherReeve.org*. Thank you for your support.