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# Using stem cells to treat ALS

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**WHAT WAS THIS ARTICLE ABOUT?** In their article “Transplantation of spinal cord–derived neural stem cells for ALS: Analysis of phase 1 and 2 trials,” Glass et al.<sup>1</sup> set out to study a specific question: Is the injection of human spinal cord–derived neural stem cells (HSSC) into a human spinal cord safe? They also wanted to know if this specialized procedure could be safely performed at multiple surgical centers by different surgeons. Small studies like this are important: they often pave the way for larger studies. In addition, before a study can be done to determine whether stem cells can be used to treat amyotrophic lateral sclerosis (ALS), the safety of the treatment must be assessed. Therefore, the results of this study are critical: these results help to decide whether larger studies of stem cells in the treatment of ALS should be done.

Why do researchers think this intervention is promising for patients with ALS? Several studies have already been done in rodents with ALS. The studies have shown that the injection of stem cells into the spinal cord delayed the onset of ALS and improved survival.<sup>2</sup> These results have prompted researchers to initiate studies in people. Glass et al.<sup>3</sup> published the results of their phase 1 trial showing that a single concentration of HSSC could be injected safely into the spinal cord. However, many questions still remained. Can increasing doses of stem cells be injected safely? Can surgeons at different institutions be trained to carry out this procedure safely? How many injections can be administered safely? How many surgeries can patients undergo safely? These were some of the questions this study tried to answer.

**HOW WAS THE STUDY DONE?** The study was performed at 3 academic medical centers. A total of 15 participants with ALS were divided into 5 treatment groups. Groups 1–5 received an increasing number of cells per injection and number of injections. One group also underwent 2 surgeries where stem cells were injected into 2 different levels of the spinal cord, both the cervical (neck) and lumbar (lower back) region. The participants were assessed for side effects or complications of the injection procedure.

In addition, each person was carefully monitored for progression of ALS. This is critical. In order for a procedure to be safe, it must meet 2 criteria. First, it must not make the disease worse. Second, it must cause few side effects. In the study by Glass et al., every person received the stem cell injections. The authors compared this group to a similar group of people who had ALS, but who did not receive the stem cell treatment. The untreated people with ALS were derived from 3 previous studies in ALS.

**WHAT WERE THE RESULTS OF THE STUDY?** Glass et al. showed that there were no differences in terms of progression of disease between those who received the stem cells and those who did not. In other words, the stem cell transplantation did not have a negative effect on the health of participants. The majority of side effects were related to the procedure to implant the stem cells. For instance, some people had pain after the surgery. Others had side effects from the immunosuppressant medications that were given after the procedure. These medications were necessary to suppress the immune system so that the body would not reject the newly implanted stem cells. In short, Glass et al. found that stem cell implantation can be safely done at high doses. Based on these findings, the transplantation of HSSC into the spinal cord can be safely expanded to include many surgical centers. This allows for future clinical trials to assess the efficacy of this procedure in the treatment of ALS.

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## About ALS

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**WHAT IS ALS?** Amyotrophic lateral sclerosis (ALS) is a progressive neurologic disease that attacks nerve cells in the spinal cord. These nerve cells, also called anterior horn cells or motor neurons, are responsible for muscle control. The nerve cells and the muscle cells work very closely together. When the nerve cell dies, as in ALS, the muscle cell also dies. This is why ALS, which affects nerve cells, causes muscle weakness in the face, arms, and legs. Lou Gehrig, who was a 7-time all-star baseball player (New York Yankees, 1923 to 1939), developed ALS. For this reason, many people call ALS “Lou Gehrig’s disease.”

ALS affects more than 12,000 people in the United States. One estimate is that ALS occurs in about 4 out of 100,000 people, according to the National Institute of Neurological Disorders and Stroke fact sheet on ALS. It happens most often between the ages of 40 and 70, with an average age of 55. It is more common in men, and is more common in whites than other races or ethnic backgrounds. About 90%–95% of cases are random; 5%–10% are genetic. In other words, about 1 in 10 cases of ALS is inherited.

The symptoms of ALS vary from person to person. Muscle weakness is the first sign. It starts very slowly, and can often be overlooked when it begins. Each person is different, so the muscle weakness can start in any part of the body. When it starts in the hand, a person may have trouble holding things, or difficulties writing. When it starts in the leg, tripping or stumbling while walking can occur. If it involves the face or mouth, swallowing can become a problem.

ALS is progressive: it gradually gets worse. Over time, more muscles become involved. Eventually, a person may not be able to walk or get out of bed. When swallowing is affected, a person may not be able to eat, and cannot maintain weight. If breathing muscles are affected, the person might need the help of a ventilator.

A neurologist may suspect ALS based on a person’s physical examination. Neurologists are trained to look for the specific physical abnormalities that ALS can cause. Medical tests, like EMG and MRI, can help to make the diagnosis and eliminate other illnesses that can look similar to ALS. Serum tests can also help: some viral illnesses that look like ALS can

show up on a simple blood test. If an inherited form of ALS is suspected, genetic testing can show that the person carries one of the genes that has been associated with ALS.

As of 2016, there is no cure for ALS. One medication, riluzole, was approved by the Food and Drug Administration in 1995 for the treatment of ALS. Riluzole is thought to reduce damage to the motor neurons. Clinical trials showed that riluzole prolongs survival by several months. The medication also extends the time before an individual needs ventilation support. Riluzole does not reverse the damage already done to motor neurons. It might cause side effects. People who are taking riluzole need to have routine blood tests looking for liver problems due to the drug. In addition to medication, people with ALS may require medical devices. These devices help to maintain mobility or, when needed, breathing.

**WHAT ARE STEM CELLS?** In recent years, stem cell research has been in the news media. Many reports have focused on the ability of stem cells to treat spinal cord injury. In 2008, it was reported that stem cells helped mice to walk better after a spinal cord injury.<sup>4</sup> In 2006, a study described how motor neurons derived from stem cells could be transplanted in mice.<sup>2</sup> In the mice who received the stem cells (and other medicines), neurologic function was partially restored. Although there is a long way to go, this kind of research might provide insight into ways of restoring nerve function after injury.

The focus on stem cells is due to their unique qualities. Stem cells can turn into any kind of cell they want. This makes them potentially very useful. For instance, if nerve cells were injured, like in spinal cord injury, it might be possible to regrow the damaged nerve cells, and restore neurologic function. ALS affects the motor neurons, which live in the spinal cord. If it is possible to implant stem cells into the spinal cord of someone with ALS, they might replace the damaged motor neurons, and restore the lost neurologic function.

Although stem cells have the potential to cure many illnesses, stem cell research is controversial. The reason is that one type of stem cell is obtained from embryos. Human stem cells come from human

embryos. The embryos must be killed in order to obtain the stem cells. The debate is an ethical one: When does life begin? Is killing an embryo the same as murder? Can an embryo be destroyed if it can save millions of lives? It is likely that these debates will continue for many years.

Although the debate centers around embryos, there are types of stem cells that do not come from embryos. Most current research focuses on the use of these types of stem cells. Much has been learned in recent years. However, we are just seeing the beginnings of this kind of research. Much more work must

be done before stem cell–derived medical treatments are available.

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