

Amyotrophic Lateral Sclerosis

Making a Difference Today

The progressive neurological disease amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, takes a quick toll on sufferers. At first, people may notice muscle weakness, twitching, or cramping. The disease then progressively disables a person's ability to walk, talk, or swallow and, ultimately, to breathe. Many spend their last days completely unable to move, while their minds remain alert. Most ALS patients die within three to five years of first experiencing symptoms, usually in midlife. And as ALS progresses, it can make increasingly heavy demands on family members and on a family's finances. Each year, the disease costs Americans some \$300 million.

ALS wreaks havoc by harming nerve cells in the brain and spinal cord that control muscles. As these nerve cells sustain increasing damage, muscles go unstimulated and waste away. Famously, the disorder took the life of Lou, known as "The Iron Horse," Gehrig, first baseman for the New York Yankees, in 1941.

Each year, doctors in the United States diagnose 5,000 new ALS cases. Once, they could do little to help these patients. But now, following years of study—much of it federally funded basic research—a drug is available that can prolong patients' lives, and scientists are finding ways to protect cells and help delay the progression of ALS.

A Fruitful Decade

Government-funded ALS research produced a number of important findings in the early 1990s. First, researchers were able to start pinning down how the disease progresses by identifying the role of the potentially toxic amino acid glutamate. ALS sufferers tend to have higher levels of this chemical messenger in certain parts of their body, and scientists have noted that nerve cells exposed to high concentrations of glutamate over a long time start to die.

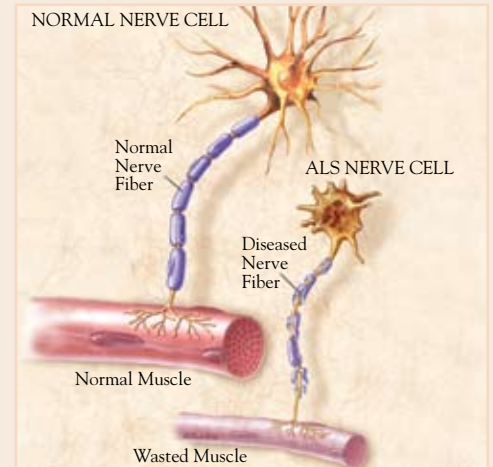
Researchers were able to use this basic research discovery to develop riluzole, an anti-glutamate drug that was shown to extend the lives of ALS patients. The first drug known to change the course of the disease, it was approved by the Food and Drug Administration in 1995.

In addition, in 1993, researchers supported by the National Institutes of Health (NIH) identified a genetic component in the hereditary form of the disease and, based on this, were able to take the crucial step of developing an animal model for ALS. This has allowed researchers to advance their study of the disease and to test dozens of potential treatments. About 20 percent of inherited cases of ALS stem from problems with this one gene, and scientists have recently identified several other genetic sources of the disease. They also are working toward pinpointing a biomarker, or biological signature common to all people with ALS, which could lead to better tools for diagnosing ALS.

Improving on Drug Treatment

While riluzole treatment can extend patients' lives, its effects are modest. Continued funding for basic research, however, could open the way to more effective treatments. Already, for example, studies show that growth factors, which function to protect cells and help them grow, and stem cells, which can divide repeatedly and assume the function of any type of cell in the body, hold promise for treating ALS.

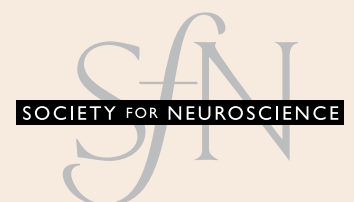
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ALS attacks nerve cells in the brain and spinal cord that control the muscles of the body. When the damaged nerve cells can no longer stimulate the muscles, they weaken and waste away. As a result, the brain and spinal cord lose their ability to initiate and control movement.

Continued funding for research could lead to:

- The discovery of the biological signature of the disease, which could lead to a diagnostic test.
- More potent therapies.
- A better understanding of how to best battle ALS and similar disorders marked by nerve cell damage.



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Amyotrophic Lateral Sclerosis

Making a Difference Tomorrow

Despite striking advances in research and treatment, the progressive neurological disorder amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, remains mysterious and debilitating.

Did you know that:

- ALS is one of the most common movement disorders. As many as 20,000 people in the United States have ALS, according to the National Institute of Neurological Disorders and Stroke, and some 5,000 new cases are diagnosed each year.
- ALS may strike anyone, and typically attacks people in midlife.
- ALS costs Americans about \$300 million annually.

Basic research into this debilitating disease funded by the National Institutes of Health (NIH) has laid the groundwork for promising advances that scientists are pursuing today.

Research Brings Hope for the Future

Already, studies funded by NIH and others have brought to light mechanisms by which ALS progresses and have led to the development of the first drug shown to affect its progress, riluzole.

Researchers suspect that they may be able to improve on riluzole with additional techniques such as the use of growth factors, special substances that appear to protect cells, which could head off the neurodegenerative decline of ALS.

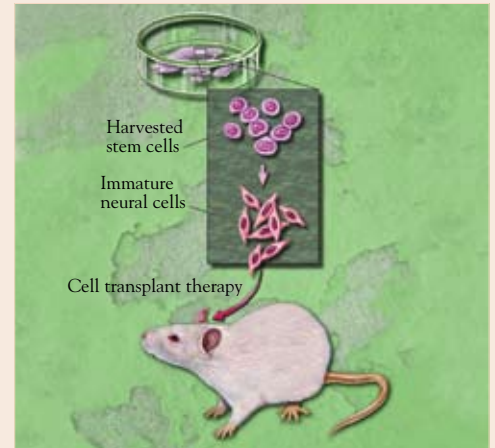
Following positive animal research, federally funded scientists are pursuing research with the growth factors IGF-1 and VEGF. They are also focusing on delivery systems that can ensure such factors arrive at the site where they will be most effective. One of these is gene therapy, in which a special system delivers growth factor-producing genes to needy cells. Recent studies revealed that gene therapy techniques involving either IGF-1 or VEGF greatly increased the survival of animal models of ALS, possibly equaling years in human life. Human studies, needed to confirm results, are now under development.

In more preliminary work, researchers are examining the use of unspecialized cells, termed stem cells. These unique cells may aid ALS in different ways. Scientists imagine stem cells could be a source of developing nerve cells that could be used to rebuild cell networks damaged by ALS. In addition, research indicates that stem cells naturally produce growth factors, which could potentially help protect cells under assault by ALS. Some researchers also are testing the use of stem cells altered to produce excess growth factors to see if they can further boost benefits.

Hope for Other Diseases

Together, these advances have made scientists optimistic that they might someday be able to further help people with ALS, or even free them from it. Findings that advance ALS research could also contribute to the understanding of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease, which share certain characteristics with ALS.

Further NIH funding will support advances in these areas, improving the lives of many Americans.



Researchers are examining therapies that involve transplanting stem cells into the brain, where they would develop into healthy nerve cells and restore cell networks damaged by ALS.

Already research has led to:

- The identification of an important genetic component of ALS, which has led to the development of better research tools.
- The first drug known to change the course of the disease.
- Important clues clarifying how ALS progresses.

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