

# NIH News in Health

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## Advances in ALS Unraveling Its Causes and Finding Treatments

Getting a diagnosis of amyotrophic lateral sclerosis (ALS) is devastating. ALS causes your muscles to weaken over time and eventually leads to death. It's also called Lou Gehrig's disease.

"ALS is a motor neuron disease," says Dr. Rita Sattler, an ALS expert at the Barrow Neurological Institute. "Motor neurons connect to every muscle in your body and control muscle movement. So if these cells are no longer there, the muscles degenerate, strength disappears, and people become fully paralyzed."

People with ALS usually die from respiratory failure. The muscles that control their breathing eventually shut down. The average lifespan of a person after they're diagnosed is three to five years.

Over the past decade, researchers have uncovered more molecular clues about how ALS develops. They're hoping this will eventually help identify people with ALS sooner. Scientists are also looking for ways to better track and treat the disease.



**Uncovering Causes** • Most cases of ALS are sporadic. That means there's no known cause. But it can also run in families. **Genetic** causes account for about 15% or less of ALS cases.

"The first genetic cause of ALS was discovered nearly 30 years ago, with a gene called SOD1," says Dr. Michael Ward, an NIH neurologist and genetics researcher. "Now, there are over 50 different genes that the research community has identified that can independently cause familial forms of ALS."

Gene mutations, or changes, can cause problems in the function of the proteins made from those genes. Most of the gene mutations found in ALS lead to the dysfunction of a protein called TDP-43. TDP-43 is important for turning your DNA, which holds your body's genetic

blueprint, into RNA. RNA is the molecule that tells your cells how to make proteins.

To work properly, TDP-43 must be in the part of the cell that houses your DNA, called the nucleus. In ALS, TDP-43 leaks out and clumps together outside of the nucleus.

"So, we have two bad things happening at the same time," Sattler explains. "We have these proteins lacking in the nucleus, and they don't do what they're supposed to be doing in the nucleus. At the same time, we have them clumping outside

the nucleus and adding even more problems to the degeneration that is already happening."

Both Sattler's and Ward's teams are studying how this protein moves in and out of the nucleus. Other NIH-funded researchers are looking for more cellular defects common to people with ALS. A better understanding of these molecular pathways may help lead to earlier detection and treatment for the disease.

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### Definitions

#### Genetic

Having to do with genes, stretches of DNA you inherit from your parents. Genes can affect your risk for certain diseases.

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**Detecting ALS Early** • Right now, getting an ALS diagnosis takes time. “In many people, it can take up to 18 months to get a final diagnosis,” says Dr. Jordan Green, a speech-language pathologist at the MGH Institute. “Early diagnosis is particularly important in a disease like ALS because the motor neurons are dying, and you want to intervene as early as possible.”

If you show signs of ALS, your health care provider will perform a physical exam and review your medical history. They may also run tests to rule out other conditions.

“But, there is no blood test that we can run that says yes, you have ALS,” says Sattler. A neurologist can assess your muscle strength, reflexes, and other functions. These tests are used to give a “functional score.” The score helps clinicians monitor the severity and progression of the disease.

One function ALS often changes is your speech. You may start speaking more slowly and have longer pauses between words. Green’s team is developing computer-based tools to

detect these changes—even before you can perceive them yourself.

One technology his team is testing is a phone app. They’re comparing how well data from the app detects changes in speech compared with a clinician’s assessment. The app tracks how fast someone talks, their tone, and other components of speech. The technology may one day be able to help predict how fast a person’s speech will decline, too.

There are also speech-generating technologies that can help a person with ALS communicate as the disease progresses. “But it’s really important to see a speech pathologist very early on in the disease,” says Green. “That way, they can learn to use these devices before they lose the ability to talk.”

Green is also working on ways to train software for people who are already experiencing speech decline. Eventually, people with ALS may completely lose their ability to talk. So, other scientists are developing brain-computer interfaces that use brain activity to help interpret what a person who can no longer speak wishes to say.

### Tracking and Treating ALS •

Scientists are seeking ways to track and slow the progression of ALS, too. Current drugs can treat a person’s symptoms but can’t stop the disease from getting worse.

Finding biomarkers—molecules or other signs of a disease—that can be used to track the progression of a disease has become a key research focus. Biomarkers can be used to see whether potential new drugs are working. NIH-funded researchers are looking at many different possibilities.

Green notes that speech detection technologies might be used as



### Wise Choices Early ALS Symptoms

- Muscle twitches in the arm, leg, shoulder, or tongue.
- Muscle cramps.
- Tight and stiff muscles, called spasticity.
- Muscle weakness affecting an arm, a leg, the neck, or diaphragm.
- Slurred and nasal speech.
- Difficulty chewing or swallowing.

a marker to test drugs. Another possibility is the TDP-43 protein. Ward’s team is testing ways to measure when TDP-43 becomes dysfunctional in cells but before it has done damage. That would allow them to see if treatments can prevent or slow the protein from doing damage.

Another potential biomarker researchers have been investigating is called neurofilament light chain. It’s a molecule that’s released when nerve cells die. A new drug is under U.S. Food and Drug Administration review for treating ALS based on its effects on this molecule. The drug is called tofersen. It targets mutated SOD1 genes. However, it’s still unclear whether the drug’s effects on the biomarker will translate into an impact on the disease.

“This is a very, very challenging disease to develop effective therapies against,” says Ward. “But we have never been in a better position from a research standpoint to begin to understand what causes ALS and how to reverse that.” ■

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Links

For more about ALS, see “Links” in the online article: [newsinhealth.nih.gov/2023/05/advances-als](https://newsinhealth.nih.gov/2023/05/advances-als)

# Hydrating for Health

## Why Drinking Water Is So Important

About two-thirds of your body weight is water. All your cells need water to work. Water is also the base for all your different body fluids, including saliva, blood, urine, sweat, and joint fluid. No living thing can survive without water. How do you know if you're drinking enough?

Your body loses water when you sweat, go to the bathroom, and even when you just breathe out. So, you need to drink enough water to replace what you lose. When you don't drink enough water, you can become dehydrated.

Signs that you're getting dehydrated include feeling very thirsty and having headaches. Your mouth or skin may feel very dry. And your urine may get darker because your body is trying to conserve water. Drinking fluids should be enough to relieve mild dehydration.

If dehydration becomes severe, it can cause confusion, fainting, an

inability to urinate, and rapid heartbeat and breathing. At this point, it can be life-threatening, and you should seek medical help fast. Drinking liquids may not be enough to replenish your body's fluids. You may need to be given fluids intravenously—through a needle or tube inserted into a vein.

Recent NIH-funded research suggests that avoiding dehydration may not be the only reason to make sure you drink enough fluids. Dr. Natalia Dmitrieva, a heart researcher at NIH, has studied the long-term effects of not drinking enough water. In one study, her team found that middle-aged people who were not adequately hydrated were more likely to develop chronic diseases. The diseases included heart failure, diabetes, chronic lung disease, and dementia.

These people were also more likely to age faster and die younger. So, staying well hydrated might help you stay healthier as you get older.

The best way to avoid dehydration is to make sure you drink enough fluids every day. Ideally, you should get your fluids from water or other low-calorie beverages, such as plain coffee or tea, or sparkling or flavored waters. Nutritional beverages, such as milk or milk alternatives, or 100% vegetable juice, are also good options. Relying on soda, sports drinks, or other sugary beverages for most of your fluids can add many calories to your diet, and they have little nutritional value.

How much you should drink each day depends on many factors, including your age, where you live, and your body weight. And your body doesn't always lose water at



the same rate. For instance, when you exercise or are active in hot weather, you sweat more and so need to drink more. But experts generally recommend drinking around 9 cups of fluids a day for women and 13 cups for men on average.

Certain diseases, like diabetes or chronic kidney disease, and some medicines can make you urinate more often. You also lose a lot of water when you throw up or have diarrhea or a fever. In these cases, you need to drink more water to avoid getting dehydrated.

Dmitrieva has changed her own drinking habits based on the results of her research. "When I started to see the results of these studies and then started seeing how much I drink, I realized that I drank less than needed," she says. "Then I just started to take one liter of water with me when I go to work. And I make sure that during the day I drink this one liter."

If you're concerned that you're not drinking enough fluids, you can take steps to stay more hydrated. See the Wise Choices box for tips. ■



### Wise Choices

#### Tips for Staying Hydrated

- Drink when you feel thirsty, if not before.
- Get your fluids from water or other low-calorie beverages, such as plain coffee or tea, or sparkling or flavored waters.
- Carry a bottle of water and refill it as needed during the day.
- Drink at regular times. For example, drink with meals.
- Drink water before, during, and after exercise.
- Drink extra fluids during hot weather or when you are sick.
- Get medical help right away if you experience confusion, fainting, rapid heartbeat or breathing, or can't urinate.



### Web Links

For more about hydration, see "Links" in the online article: [newsinhealth.nih.gov/2023/05/hydrating-health](https://newsinhealth.nih.gov/2023/05/hydrating-health)





## Health Capsules

For links to more information, please visit our website and see these stories online.

### Artificial Pancreas Helps Kids With Diabetes

In type 1 diabetes, your body mistakenly attacks and destroys certain cells in your own pancreas. These cells normally make a molecule called insulin. Without insulin, the sugar glucose builds up in your blood. This can cause serious health problems.

Current treatments for type 1 diabetes include frequent testing of blood glucose and insulin injections. But researchers have been working on a new approach called artificial pancreas systems. These automated systems contain a blood glucose monitor and an insulin pump. The

monitor provides constant feedback to the pump. The pump then supplies insulin to the body when needed.

Past studies showed that such systems work well in adults and older children. Scientists tested an artificial pancreas system in 68 children, ages 2 to 5, with type 1 diabetes. They compared their blood glucose levels with those of 34 children receiving standard care.

After three months, children with the artificial pancreas showed more stable blood glucose levels than the kids getting standard care. They had about three more hours per day

of better blood glucose control. The benefits were greatest during the night, when kids would be sleeping.

“Artificial pancreas systems have the potential to improve all-day blood glucose control in these young patients,” says NIH diabetes expert Dr. Guillermo Arreaza-Rubín. “This could help ease concerns about the long-term effects of type 1 diabetes on children’s health.”

More study is needed to see how well the artificial pancreas system works in young kids over long periods of time. ■

### Complementary Health Approaches for Pain Relief

Pain is the most common reason people seek medical care. Many also look to complementary health approaches. But how do you know if they’re safe and helpful?

To help you find answers, NIH has a free e-book called “Pain: Considering Complementary Approaches.” It summarizes the evidence behind different complementary approaches for pain relief. These include acupuncture, massage therapy, spinal

manipulation, and more. There’s also a chapter on music-based interventions for pain relief. Download the PDF of this free 50-page e-book at [www.nccih.nih.gov/health/pain-considering-complementary-approaches-ebook](http://www.nccih.nih.gov/health/pain-considering-complementary-approaches-ebook).

NIH also has more information online about complementary approaches for chronic pain. Chronic pain is pain that lasts for three months or longer. It affects an estimated 1 in 5

adults in the U.S. Some studies have shown that certain complementary approaches can help relieve chronic pain. Examples are yoga, hypnosis, and mindfulness meditation. You can learn about the evidence for treating different types of chronic pain, including back and neck pain, headaches, and fibromyalgia.

Read more at [www.nccih.nih.gov/health/chronic-pain-what-you-need-to-know](http://www.nccih.nih.gov/health/chronic-pain-what-you-need-to-know). ■



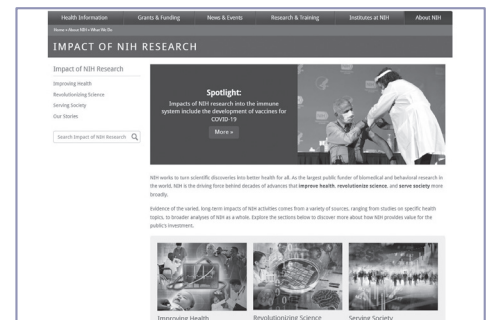
### Featured Website

#### Impact of NIH Research

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