Prolonged fasting 're-boots' immune system

Results of a new study on mice and a phase 1 trial of humans suggest that prolonged cycles of fasting – for 2-4 days at a time – not only protect against toxic effects of chemotherapy, but also trigger stem cell regeneration of new immune cells and clearing out of old, damaged cells.

The study, by researchers from the University of Southern California (USC) in Los Angeles, and published in the journal *Cell Stem Cell*, is the first to show that a natural intervention can trigger regeneration of an organ or system through stem cells.

The team believes the findings could benefit people with immune system damage, for example if they have received chemotherapy as treatment for cancer. It could also benefit the elderly because immune systems are weakened through aging, making them more susceptible to disease.

The scientists say prolonged fasting appears to shift stem cells of the immune system from a dormant state to an active state of self-renewal.

Results from experiments with mice and a phase 1 human clinical trial showed that long periods of fasting significantly lowered levels of white blood cells. In the mice, it flipped a switch that changed the signaling pathways of hematopoietic stem cells – a group of stem cells that generate blood and immune systems.

"We could not predict that prolonged fasting would have such a remarkable effect in promoting stem cell-based regeneration of the immune system," says Valter Longo, a professor of Gerontology and the Biological Sciences at the USC Davis School of Gerontology, and director of the USC Longevity Institute.

He says that when you stop eating, the body uses up stored glucose, fat and ketones, and also recycles worn out and damaged immune cells.

"What we started noticing in both our human work and animal work is that the white blood cell count goes down with prolonged fasting," he explains, "Then when you re-feed, the blood cells come back. So we started thinking, well, where does it come from?"

In mice, prolonged fasting replenished worn out immune cells with new ones

The researchers found that fasting for 2-4 days reduced PKA, an enzyme that is involved in extending lifespan in simple organisms.

In mice, prolonged periods of fasting – repeated cycles of 2-4 days with no food – over the course of 6 months, killed older and damaged immune cells and generated new ones.

During each fasting cycle, the drop in white cell levels triggered a stem-cell based regeneration of new immune cells. In particular, prolonged fasting reduced PKA, an enzyme that the team had previously discovered is involved in extending lifespan in simple organisms.

Other studies have also linked PKA to the control of stem cell self-renewal and pluripotency – the extent to which they can become different cell types.

Prolonged fasting also led to a drop in IGF-1, a growth factor hormone linked to aging, cancer and tumor progression.

Switching off the gene for PKA is the key step that triggers the stem cells to shift to regeneration. Prof Longo says, "It gives the OK for stem cells to go ahead and begin proliferating and rebuild the entire system."

And the good news, he adds, is that the body also rids itself "of the parts of the system that might be damaged or old, the inefficient parts, during the fasting. Now, if you start with a system heavily damaged by chemotherapy or aging, fasting cycles can generate, literally, a new immune system."

Three-day fast protected cancer patients from toxic chemo effects

In a clinical trial involving a small group of cancer patients, the team also found that fasting for 3 days before receiving chemotherapy protected them from its toxic effects.

While chemotherapy saves lives, it also causes significant damage to the immune system, and the team hopes their findings show that fasting may help to minimize some of that harm.

Meanwhile, there is no suggestion that people should try to get these same effects by prolonged fasting, which should only be done under medical supervision.

More clinical studies are now needed to test the effectiveness of the approach in humans and also examine the side effects.

Prof. Longo says they are now investigating whether these same regeneration effects work with other systems and organs as well as the immune system. His lab is already planning further animal studies and clinical trials.

Funding from the National Institute of Aging of the National Institutes of Health (NIH), the V Foundation and the Longevity Institute at USC Davis School of Medicine.

Meanwhile, *Medical News Today* recently reported how stem cells show potential for brain damage repair. Research from Australia suggests by manipulating cell-surface proteins it may be possible to get bone marrow stem cells to differentiate into brain cells. If the method proves viable, it could lead to ways of generating new brain cell populations for repairing brain damage.

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How the immune system watches over the brain

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- **Scientists have long puzzled over how the immune system surveils the brain when the blood-brain barrier prevents immune cells from entering.**
- **A study has now identified border "checkpoints" where the immune system monitors fluid leaving the brain for signs of infection.**
- **The discovery offers new possibilities for treating brain diseases, such as multiple sclerosis (MS).**

Generations of students have learned that the central nervous system has "immune privilege," this means that – to an extent – the immune system tolerates the presence of foreign proteins, or antigens, and tissue in the brain and spinal cord.

The immune system cannot respond in the usual way to infections, injuries, or tumors in the brain and spinal cord, because the blood-brain barrier prevents immune cells from entering or leaving.

Despite this, scientists know that inflammation plays a pivotal role in many neurological and psychiatric conditions, including Alzheimer's disease, MS, autism, and schizophrenia.

So the question remains, if there is no exchange of information, how does the immune system respond to and influence the brain in such a broad range of conditions?

A team of scientists led by Washington University School of Medicine in St. Louis, MO, have discovered that immune cells are stationed in the dura mater, which is the tough outer membrane of the brain.

From this vantage point, they monitor the cerebrospinal fluid draining from the brain. If they detect the molecular calling cards of infection, cancer, or injury, they can mount an immune response.

The research appears in the journal *Cell*.

Immunity and the brain

"Every organ in the body is being surveilled by the immune system," says senior author Dr. Jonathan Kipnis. Alan A. and Edith L. Wolff Distinguished Professor of Pathology and Immunology.

He explains:

> "If there is a tumor, an injury, an infection anywhere in the body, the immune system has to know about it. But people say the exception is the brain; if you have a problem in the brain, the immune system just lets it happen. That never made sense to me. What we have found is that there is indeed immune surveillance of the brain — it is just happening outside the brain."

In 2015, a study in mice revealed a network of vessels in the dura mater that drains cerebrospinal fluid from the brain into lymph nodes in the neck. Also in 2015, a study led by Dr. Kipnis recorded similar findings in both mice and humans.

Lymph nodes are part of an extensive network of fluid-filled vessels known as the lymphatic system. An accumulation of pathogens in lymph nodes can lead to the initiation of an immune response.

This suggested a more intimate connection between the brain and immune system than previously suspected. However, it remained unclear exactly where and how immune cells surveil the contents of the cerebrospinal fluid as it drains from the brain.

Dr. Kipnis and his colleagues knew that the lymph vessels that carry fluid from the brain run alongside blood-filled cavities, or sinuses, in the dura.

Crucially, the walls of these sinuses are more permeable than the blood vessels of the blood-brain barrier.

Following up this clue, the scientists showed in their experiments that small molecules from the brain and immune cells accumulate in the sinuses.

Some of the cells, known as antigen presenting cells, which include dendritic cells, pick up suspicious molecules and present them to other immune cells, called T cells, which patrol the body in the bloodstream.

When they bind to these suspect molecules, the T cells can initiate an immune response.

Special status

Dr. Justin Rustenhoven, a postdoctoral researcher and the first author of the new paper, says the brain must be shielded from the full force of the immune system.

"Immune activity in the brain can be highly detrimental," he says. "It can kill neurons and cause swelling. The brain cannot tolerate much swelling, because the cranium is a fixed volume. So immune surveillance is pushed to the borders, where the cells can still monitor the brain but do not risk damaging it."

Dr. Kipnis uses a metaphor to explain how immune cells in the dural sinuses monitor the contents of cerebrospinal fluid for unfamiliar proteins or antigens:

> "Imagine if your neighbors went through your trash every day. If they start finding blood-stained towels in your trash, they know something is wrong. It is the same thing with the immune system. If patrolling immune cells see tumor antigens or signs of infection from the brain, the cells know there is a problem. They will take that evidence to immune headquarters, which is the lymph nodes, and initiate an immune response."

The findings offer promising opportunities for treating brain disorders that involve autoimmune attacks on tissue.

In MS, for example, the immune system degrades the myelin sheath, which is the fatty insulating material that protects nerve cells.

Future treatments could target immune cells in the sinuses of the dura mater to prevent them from initiating certain immune responses in the brain.

"Now that we know where it is happening, that opens up lots of new possibilities for modulating the immune system," says Dr. Kipnis.

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What to eat and avoid to maintain a strong immune system

Medically reviewed by Kim Rose-Francis, RDN, CDCES, CNSC, LD, Nutrition — By Veronica Zamora
Updated on May 6, 2021

Foods to avoid | Foods to eat | Summary

The immune system helps protect the body against contractable illnesses, such as a cold and the flu. Nutrition is an important part of ensuring that the immune system stays strong.

Regularly consuming some unhealthy foods may prevent the immune system from functioning properly. This may reduce how quickly the ability to function as well as it could.

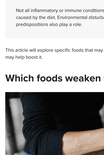
Some research suggests that diets high in added sugar and excess salt are associated with an increased risk of certain autoimmune conditions and other chronic illnesses.

On the other hand, eating foods that contain certain nutrients, such as vitamin C, may help boost the immune system.

> Not all inflammatory or immune conditions, including obesity and type 2 diabetes, are caused by the diet. Environmental disturbances, medications, and genetic predispositions also play a role.

This article will explore specific foods that may weaken the immune system and others that may help boost it.

Which foods weaken the immune system?



Louise Fathe/Offset

Anyone looking to support their immune function may want to limit or avoid the following types of foods:

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of foods.

Processed foods

Many processed foods contain unhealthy fats, sugars, and additives. These can improve a product's taste, texture, and shelf life, but as the studies below suggest, they may weaken the immune system.

Some processed foods with high amounts of additives include:

- canned foods
- microwaveable meals
- chips
- cakes and cookies

One 2017 study [1] found that eating foods containing additives may increase the risk of several chronic inflammatory or metabolic conditions. The study looked at additives such as sucralose, aspartame, carboxymethylcellulose, polysorbate-80, sodium, and carrageenan.

The researchers also observed that people with diets high in additives are more likely to have obesity, immune-related inflammation, and insulin resistance.

Meanwhile, a 2014 review [2] of studies noted that a high intake of salt, refined sugar, saturated fat, and omega-6 fatty acids, along with a shortage of omega-3 fatty acids, can damage the immune system.

Eating sugars and fats in processed foods might also lead to an overconsumption of calories, which can increase the risk of obesity. Obesity can lead to inflammation, which can lead to [3] insulin resistance, as well as immune system dysregulation.

Foods high in sugar

People with high sugar diets have an increased risk [4] of several chronic conditions, including coronary heart disease and type 2 diabetes.

Some foods that tend to be high in sugar include:

- preserves, marmalades, and sweets
- cookies and cakes
- flavored milk and sweetened dairy products
- sugary breakfast cereals
- sugary drinks, such as soda

Also, eating a diet high in sugar may limit the immune system's ability to combat disease. It may do this by reducing the effectiveness of white blood cells and increasing inflammation.

Foods high in refined carbohydrates

Foods that are processed and high in refined carbohydrates, such as white flour and refined sugar, are associated with increases in inflammation and oxidative stress, which can harm the immune system.

Some foods that contain refined carbohydrates include [5]:

- white rice
- white bread
- sweets, cookies, and cakes made with white flour

Foods for a healthy immune system

Having a well-rounded, nutrient-dense diet can help with maintaining a moderate body weight, which is important [6] for immune system function.

The following foods may provide more specific immune-boosting benefits.

Citrus fruits

These are good sources of vitamin C, and a 2017 study [7] found that vitamin C has several properties that can contribute to healthy immune function.

Vitamin C is a powerful antioxidant. Antioxidants protect important molecules in the body, such as proteins and carbohydrates, from environmental and biological damage.

Vitamin C also helps promote metabolic energy and hormone regulation, and it is necessary for collagen production.

The same 2017 study reported that most people should aim to consume 100–200 milligrams (mg) of vitamin C per day.

Foods that contain zinc

Zinc is an essential mineral that is key [8] for maintaining a healthy immune system.

The recommended daily intake of zinc ranges from 2–14 mg [9], depending on a person's age and sex. When a person is pregnant, they need 11–12 mg.

Some dietary sources of zinc include:

- oysters
- beef
- baked beans
- fortified cereals
- chicken breast
- cheese
- pork

Cruciferous vegetables

These vegetables, especially broccoli and broccoli sprouts, are good sources of the compound sulforaphane, which may help boost the immune system.

One 2016 study [10] observed that sulforaphane has antioxidant, anti-inflammatory, and anticancer properties.

A 2018 study [11] investigated the effect of sulforaphane on colon cancer cells. It found that sulforaphane prevented inflammation of the immune cells, which the researchers suggested may help prevent the development of cancer.

Ginger

People have been using ginger to add flavor for centuries. More recently, researchers have investigated its effects on the immune system.

A 2020 analysis [12] of high-quality studies found that consuming ginger supplements combatted inflammation associated with osteoarthritis and rheumatoid arthritis.

The analysis also found that ginger supplements helped reduce body weight in people with obesity. This may mean that ginger also improves the health of the immune system indirectly, as obesity is linked [13] with chronic inflammation.

Summary

Anyone looking to support their immune system might want to limit their intake of foods high in refined carbohydrates, sugar, and additives. These foods may suppress immune function.

A varied diet that is rich in nutrients, on the other hand, may boost the immune system and help reduce inflammation.

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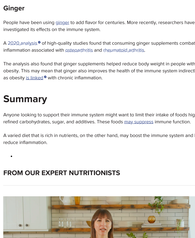

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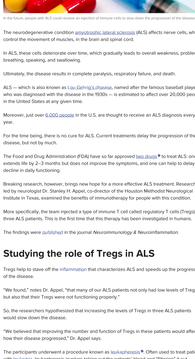
ALS: Immune cells may slow disease progression

A new study brings hope for people with ALS. Immunotherapy may dramatically slow down the progression of the disease, it shows.



In the future, people with ALS could benefit from injections of immune cells to slow down the progression of the disease.

The neurodegenerative condition amyotrophic lateral sclerosis (ALS) affects nerve cells, which control the movement of muscles, in the brain and spinal cord.

In ALS, these cells deteriorate over time, which gradually leads to overall weakness, problems breathing, speaking, and swallowing.

Ultimately, the disease results in complete paralysis, respiratory failure, and death.

ALS — which is also known as Lou Gehrig's disease, named after the famous baseball player who was diagnosed with the disease in the 1930s — is estimated to affect over 20,000 people in the United States at any given time.

Moreover, just over 6,000 people in the U.S. are thought to receive an ALS diagnosis every year.

For the time being, there is no cure for ALS. Current treatments delay the progression of the disease, but not by much.

The Food and Drug Administration (FDA) have so far approved two drugs [14] to treat ALS: one extends life by 2–3 months but does not improve the symptoms, and one can help to delay the decline in daily functioning.

Breaking research, however, brings new hope for a more effective ALS treatment. Researchers led by neurologist Dr. Stanley H. Appel, co-director of the Houston Methodist Neurological Institute in Texas, examined the benefits of immunotherapy for people with this condition.

More specifically, the team injected a type of immune T cell called regulatory T cells (Tregs) into three ALS patients. This is the first time that this therapy has been investigated in humans.

The findings were published in the journal *Neuroimmunology & Neuroinflammation*.

Studying the role of Tregs in ALS

Tregs help to stave off the inflammation that characterizes ALS and speeds up the progression of the disease.

"We found," notes Dr. Appel, "that many of our ALS patients not only had low levels of Tregs, but also that their Tregs were not functioning properly."

So, the researchers hypothesized that increasing the levels of Tregs in three ALS patients would slow down the disease.

"We believed that improving the number and function of Tregs in these patients would affect how their disease progressed," Dr. Appel says.

The participants underwent a procedure known as leukapheresis [15], often used to treat patients with leukemia, leukapheresis involves taking out the patients' blood and "filtering" it out through a special machine that separates the white blood cells from the red ones.

In this case, the researchers separated Tregs from the red blood cells and expanded them ex vivo. After that, the red blood cells were returned to the bloodstream.

The researchers noticed that in the case of the patients whose Tregs weren't functioning properly, once the cells were outside the body, they returned to normal.

Throughout the study, the patients received eight Treg injections, and their disease progression was assessed using two different ALS progression rating scales.

'From a death sentence to a life sentence'

First study author Dr. Jason Thonhoff, Ph.D., a Houston Methodist neurologist, further details the research and reports on the findings. He says, "A person has approximately 150 million Tregs circulating in their blood at any given time."

"Each dose of Tregs given to the patients in this study resulted in about a 30 to 40 percent increase over normal levels," Dr. Thonhoff adds.

"As we believed, our results showed it was safe to increase their Treg levels," says Dr. Appel. Dr. Thonhoff adds, "Slowing of disease progression was observed during each round of four Treg infusions."

"What surprised us," he goes on, "was that the progression of their ALS dramatically slowed while they received infusions of properly functioning Tregs."

> "My hope is that this research changes ALS from a death sentence to a life sentence. It won't cure a patient's disease, but can make a difference."
>
> *– Dr. Stanley H. Appel*

Dr. Thonhoff is also very pleased with the results and he is hopeful about future therapies. He says, "Larger studies will be required to determine whether it is an effective treatment, but as a clinician and researcher who specializes in ALS, I am very excited about the hope these initial findings provide."

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By Ana Sandoiu on May 24, 2018 — Fact checked by Jasmin Collier

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Drinks for naturally boosting the immune system: Do they work?

Do they work? | Drinks to try | Other tips | Summary

The human immune system is a complex defense system involving multiple organs and specialized cells and tissues.

Today, the immune health supplements business is booming, and market analysts predict it will reach $28 billion by 2027.

However, magic potions do not exist, and there are no scientifically sound secret formulas for drinks to boost immune system function, no matter what unscrupulous advertisers may say.

In fact, researchers maintain [16] the only real way to enhance immunity is with vaccines for specific illnesses.

The best way to boost the effectiveness of the immune system through nutrition is by eating a well-balanced diet and keeping fit overall.

Using drinks to boost immune system function may help if they are a part of a larger, nutritionally sound approach.

Do they work?

A person should eat a well-balanced diet and keep as fit to support the immune system.

Medically reviewed by Katherine Marengo, LDN, R.D., Nutrition — By Daniela Drescher on March 30, 2020

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Experts note that malnutrition is a significant cause of poor immune function. Regularly consuming drinks that contain vital nutrients may play a role in preventing illness and helping people recover from it.

Nutrients the body needs for the immune system to develop and function appropriately include:

- **Protein**: Protein and the essential amino acids play a vital role in supporting the immune system's ability to withstand and recover from an attack by infectious agents.
- **Fish oil**: Research suggests fish oil may help reduce inflammation.
- **Vitamin A**: Vitamin A helps support the immune functions, such as the mucous cells lining essential organs and the body's ability to make antibodies in response to specific infections.
- **Vitamin D**: Vitamin D stimulates the immune system and helps the formation of immune cells. A lack of vitamin D has links to a greater risk of autoimmune diseases.
- **Vitamin C**: Vitamin C supports the body's ability to produce infection-fighting white blood cells.
- **Probiotics**: Sometimes called "the good bacteria," these beneficial microorganisms promote a healthy digestive system.
- **Catechins**: Derived from plants and found in green tea, may help the immune system function.

A balanced diet containing a wide variety of vitamins and minerals is essential for immune function. Additional nutrients that support the immune system include:

- vitamin E
- vitamins B-6 and B-12
- folate
- zinc
- selenium
- iron

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Drinks to try

Beverages play a vital role in maintaining health. Simply staying hydrated is a great way to boost the immune system.

The body needs water to function effectively, and this is particularly true for the many and diverse components of the immune system.

For example, the mouth and throat are on the front lines of the body's defenses, but they cannot do their job as well as usual when a person is dehydrated.

Drinks to boost the immune system do not always have to be complex, expensive, or made in a blender.

They should, however, be non-caffeinated and low in sugar. Water is a great place to start. From there, people can choose more complex beverages to suit their needs and tastes.

Green tea, which is rich in catechins, and tomato juice, a good source of vitamin C, are good examples of drinks that contribute to a person's overall health.

Smoothies are a great way to pack plenty of nutrients into one beverage. For example, people can add the following ingredients to smoothies:

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- protein, which is in nuts, seeds, soy, and dairy products
- vitamin C, which is in oranges, strawberries, and tomato juice
- vitamin A, which is in spinach, carrots, and apricots

The Physicians Committee for Responsible Medicine recommend this smoothie. In a blender, combine the following ingredients for one minute, or until as smooth as desired:

- 1 peeled orange
- 1 cup grapes
- 1 peeled banana
- 1 cored pear
- 1 cup soy, almond, or rice milk
- 2 cups fresh kale or spinach
- ice cubes (optional)

Other tips

Although health experts are not very likely to recommend using drinks to boost the immune system, there are proven steps individuals can take to support their immune function.

These include:

- **Handwashing:** Frequent handwashing will support the immune system by removing potential contagions.
- **Not touching the face:** Keeping the hands away from the face keeps germs away from the mouth, nose, and eyes, where they can enter the body.
- **De-stressing:** Cortisol, a hormone the body produces when it is under stress, may interfere with the immune system.
- **Eating a healthful, well-balanced diet:** Eating plenty of fruits and vegetables and avoiding processed foods that are high in fat and sugar may help keep the immune system strong.
- **Getting plenty of sleep:** It is essential to give the body time to rest and recuperate. Researchers ⚲ think that lack of sleep may have detrimental effects on immune function because it interferes with the circadian rhythm.

The immune system also changes over time. Infants and young children have an immature immune system, plus significant nutritional needs to support their growth.

By adolescence and adulthood, their immune systems will be fully developed, but lifestyles might not be conducive to overall health.

Older adults have acquired substantial immunity, but their immune system may not be as strong.

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Summary

Although there are no magic drinks that can suddenly boost the immune system, certain nutrients do play a key role in disease prevention and recovery.

People should stay hydrated by drinking plenty of water. There is no evidence that drinks marketed specifically for their 'immune-boosting properties' actually work.

The most effective approach is to incorporate plenty of nutrients in the diet. People should also be sure to wash their hands, get enough sleep, and reduce stress where possible.

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