



When faced with joint pain, or even an injury, applying heat or alternating heat and cold are popular treatments that can be effective. But as we age, chronic inflammation—and enduring pain—can set in, a development so common it has a name: "inflammaging."

PHOTOGRAPH BY DRAGONIMAGES, GETTY IMAGES

PREMIUM

- [SCIENCE](#)

What is 'inflammaging'? Here's how inflammation affects you differently as you age.

As we grow older, aches and pains can become a chronic part of life. But experts say it doesn't have to—and solutions are on the way.

By Emily Sohn

December 27, 2023

It happens to everyone. With age come discomforts: achy joints, wounds that heal more slowly, and a rising risk for cancers, heart disease, dementia, arthritis, and other illnesses. Those changes follow an uptick in inflammatory molecules over the course of a lifetime, according to a large and

growing body of research. The link between age, inflammation, and disease is so well established, it has a name: inflammaging.

Now, researchers are unraveling the details of how the inflammatory process changes over the lifespan, what instigates the shift, and how it might be possible to interfere with the process. The work suggests interventions ranging from new drugs to new motivations for healthy habits like exercise that can slow the aging process, says Ron DePinho, a cancer biology and aging researcher at the University of Texas MD Anderson Cancer Center in Houston.

Research on inflammaging also illustrates the nuanced challenge of taking the reins of inflammation to sustain health later in life. Although many people fixate on the need to reduce inflammation, it is more important to sustain the appropriate amount of it as a means toward extending quality rather than quantity of life, says Judith Campisi, a cell biologist at the Buck Institute for Research on Aging, an independent research facility in Novato, Calif.

“What happens with age is you lose control of inflammation,” she says. “Even if you're five years old, you will never heal a wound without an initial inflammatory response. It's not always bad. It's sometimes good.”

Hallmarks of aging

As people age, according to numerous studies, increasing amounts of pro-inflammatory cytokines and other inflammation-related molecules circulate in the blood alongside a rise in localized inflammation. When the shift occurs depends on the person, DePinho says, but 50 is generally when inflammation starts to increase, with a dramatic shift after 60.



This x-ray shows the hands and wrists of a 54-year-old patient with rheumatoid arthritis, an autoimmune disease that causes chronic inflammation.

PHOTOGRAPH BY ZEPHYR, SCIENCE SOURCE

That uptick tracks closely with disease trends. Beginning in the early sixties, risks rise substantially for the most common chronic diseases of aging: cancer, diabetes, heart disease and dementia, DePinho says. Starting at 65, the number of people with Alzheimer's doubles every five years. In the U.S., 80 percent of adults over 65 have at least one chronic condition. By age 85, a third of people may have Alzheimer's, while a third of men and one-fourth of women have had cancer. People with more inflammation in their bodies have a higher risk of disease.

Scientists have identified a dozen biological changes that correspond with age. All of those hallmarks of aging are associated with inflammation, and inflammation is considered a pillar of aging, says Luigi Ferrucci, a geriatrician and epidemiologist at the Intramural Research Program of the NIH's National Institute on Aging in Baltimore, Maryland.

For example, as people get older, their immune cells lose their protective functions and stop doing the job of fighting off invaders, turning into what scientists call senescent cells. Other kinds of cells can also become senescent in response to stress. They cease replicating, no longer do their jobs, and start to secrete powerful inflammatory molecules that cause yet more cells to become senescent in a self-perpetuating cycle.

A relentless loop

Meanwhile, DNA damage inside cells accumulates over time, especially at the tips of chromosomes in protective regions called telomeres, which are long stretches of bunched-up DNA. Each time a cell divides, its telomeres become shorter until they reach a critical length that is perceived by the cell as DNA damage or instability, which may induce cellular senescence.

As telomeres become damaged, they initiate a signaling process through proteins that turn certain genes on and off. Some of the genes affected support the function of mitochondria (the cell components that produce energy). As a result of the gene disruption, mitochondria become defective and leak their DNA into cells, sparking inflammation.

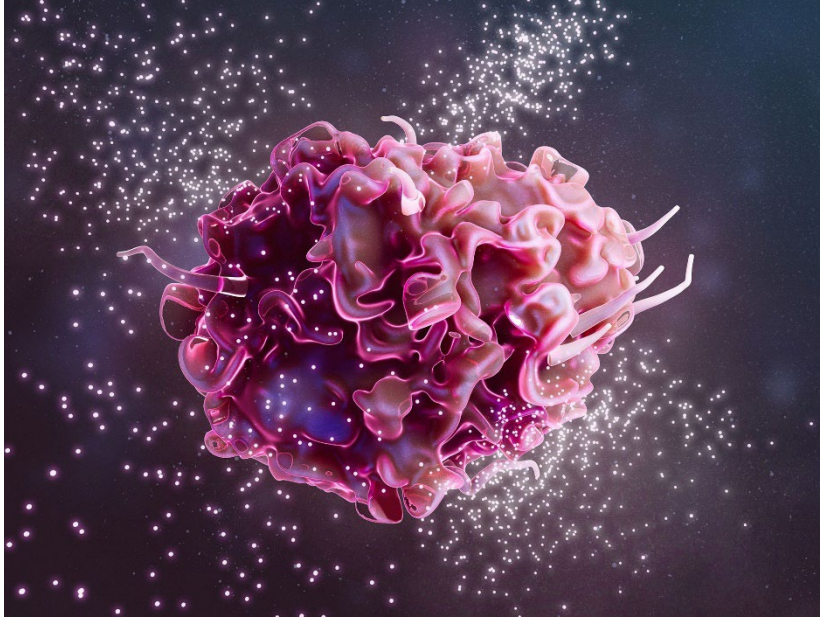
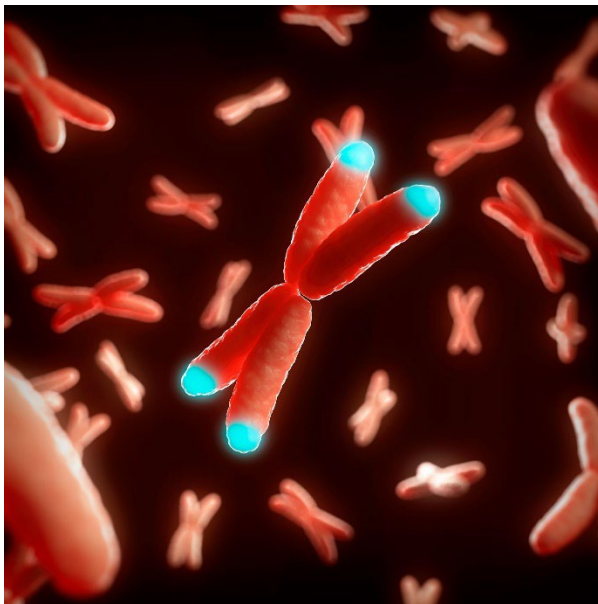


Illustration of a macrophage releasing cytokines, which promote inflammation. Macrophages are cells of the body's immune system that engulf and destroy pathogens, dead cells, and cellular debris.

ILLUSTRATION BY NANOCLUSTERING / SCIENCE SOURCE



Aging causes damage on the cellular level, much of it to telomeres, which are protective areas on the ends of chromosomes (depicted in this illustration).

ILLUSTRATION BY SCIEPRO, SCIENCE SOURCE

Scientists used to consider telomere shortening, mitochondrial damage, inflammation, and other processes as separate theories of aging that could contribute to diseases like cancer, DePinho

says. Now it is clear that all of these changes are connected and that inflammation acts like a “co-conspirator” in the aging process.

As chronic inflammation sets in, it becomes harder for the immune system to perform routine tasks, like detecting and eliminating cancer cells and pathogens, which could make people more likely to develop diseases. Inflammation in the body may also activate immune cells in the brain called microglia, according to one theory, causing inflammation, weakening the blood-brain barrier, and destroying nerve cells, ultimately contributing to the development of Alzheimer’s.

This burgeoning understanding of inflammaging as a relentless circuit of steps that all exacerbate inflammation is revealing new ways to break the cycle.

Aging better

Efforts to develop anti-aging interventions that target inflammation are challenging because they need to be specific to avoid causing more harm than good, Ferrucci says. Trying to tackle the chronic inflammation of aging with general anti-inflammatory drugs, for example, could make people more susceptible to disease by impairing the inflammation that our bodies need for staying healthy. “When you have an infection, if you don't have inflammation, you're going to die,” Ferrucci says. “Shutting down inflammation with a bomb like a corticosteroid or some monoclonal antibodies works. It's also quite dangerous.”

One of the most promising new strategies for dealing with inflammaging is attacking senescent cells, experts say. In mice, a low-dose combination of two drugs, called Dasatinib and Quercetin, appears to be particularly effective at getting rid of these deadbeat cells and reducing inflammation in the intestines with the potential to extend lives. Clinical trials are now underway with these and other so-called senolytics to see if the same kinds of compounds might kill senescent cells and break the cycle of inflammation and disease in people too, says DePinho.

Other ongoing approaches include efforts to identify drugs that could restore telomeres, enhance mitochondrial function, and activate anti-aging genes, a strategy DePinho is working on. Some over-the-counter supplements claim to boost levels of proteins called sirtuins, which help cells respond to stresses, and a molecule called NAD⁺, which helps mitochondria function, among other roles, and dwindles in half from youth to middle age. Although evidence has been seriously questioned and these products have been over-hyped, DePinho says, further study may illuminate new anti-aging properties of sirtuins.



Any activity that gets us up and moving can be effective at staving off inflammation as we age, including dancing.

PHOTOGRAPH BY LINDSAY COMER



Foods like hummus, vegetables, salad, beans, couscous, and avocado are part of a fiber-filled, anti-inflammatory diet.

PHOTOGRAPH BY KSENIYA OVCHINNIKOVA

Scientists are hopeful that they are getting closer to understanding which interventions will help most, and studies in mice illustrate the tantalizing possibilities. “Tissues retain a remarkable capacity to renew themselves if you remove the underlying instigators of the aging process,” DePinho says.

Advances in immunology are lending new insights into how we can allow good inflammation to proceed while squashing the bad that can come from too much of it, Ferrucci adds. “As we discover

the nuances of inflammation,” he says, “then it may be possible to find drugs that do not shut down inflammation completely.”

Age-fighting behaviors

For now, there are simple steps people can take to address inflammaging in their own bodies, experts say, including exercise. Regular physical activity enhances DNA repair, improves mitochondrial function, activates sirtuins, and, studies show, can reduce the risk of cancer, diabetes, heart disease, and Alzheimer’s. Regular vigorous activity is best, but as little as 15 minutes a day can make a difference, DePinho says, and even leisure activities help.

Dietary choices, too, can improve the chronic inflammatory state of inflammaging, according to a variety of studies that support eating a Mediterranean-style diet with an emphasis on whole grains, produce, nuts, and fish. Eating a wide variety of vegetables may also help sustain the gut microbiome, which tends to become less resilient and contribute to rising levels of inflammation with age. Each Saturday, when Ferrucci goes to the market to shop for the week, he buys 10 different kinds of vegetables, based on this emerging evidence. “That is something that has been suggested in the literature,” he says. “And I think that’s a simple way of following that advice.”

Body fat releases cytokines that promote inflammation, DePinho adds, so using exercise and diet to control weight can have extra benefits. He also advises people to avoid or quit smoking, a habit known to increase DNA damage and drive inflammation. Finding ways to relax is another useful goal, as chronic stress has been linked to shortened telomeres, accelerated aging, and inflammatory diseases. Adequate sleep and meditation can help reduce stress, DePinho says.

Healthy habits like these are important throughout life, Ferrucci says, but they become especially important as the mechanisms that protect our cells from damage become less functional with age. That accumulating damage is a key source of inflammation. “Intervening in any possible way becomes more important as you become older,” he says.

A version of this story appears in the [August 2024 issue](#) of *National Geographic* magazine.

Portions of this story have previously appeared in *Anti-Inflammation*, by Emily Sohn. Copyright © 2024 National Geographic Partners, LLC. [Available wherever books and magazines are sold.](#)