

■ ■ ■ A SYSTEMIC RESPONSE

A healthy immune function that gets chronically triggered can cause any number of ailments. Here's how and why inflammation happens, why it is dangerous, and simple lifestyle tips to keep your risk factors in check.

BY HOLLY PEVZNER

Inflammation is a hard concept to get your head around. After all, doctors aren't exactly in the habit of handing out inflammation diagnoses. There's no American Inflammation Society. There are no walks to raise money for inflammation research; there's no special colored ribbon to honor those who are suffering. Still, a 2019 report in the journal *Nature Medicine* noted that disease related to chronic inflammation is the most significant cause of mortality today, accounting for half of all deaths worldwide. The researchers stated that prevention, early diagnosis and treatment of severe chronic inflammation would greatly reduce those numbers.

But how do we go about preventing a condition that so many of us still don't really understand? The answer: we learn more. Here, what you need to know.

Inflammation Starts Off as a Positive

The word "inflamed" brings thoughts of red, fiery ire. And that, in a nut, is inflammation. While it sounds menacing, "inflammation in small amounts is a good thing. We need it," says Monica Aggarwal, M.D., director of integrative cardiology and prevention at the University of Florida in Gainesville and co-author of *Body on Fire: How Inflammation Triggers Chronic Illness and the Tools We Have to Fight It*. With acute inflammation, your body is angry at an invader, like an infection, a sprain or a cut. In retaliation, platelets are sent to get rid of the invader, followed by white blood cells that swoop in and "act as the cleanup crew, sweeping up debris, such as bacteria, toxins and broken proteins from damaged tissues," explains Vivian P. Bykerk, M.D., a rheumatologist at the Hospital for Special Surgery in New York City. There will be redness, swelling,





fight gets stuck in a seemingly endless loop in which inflammation causes damage to tissues in the body and that damage spurs further inflammation, and on and on. And that's called a chronic inflammatory response.

What "Disease" Is Inflammation, Anyway?

OK, so chronic inflammation isn't one specific disease. Your doctor wouldn't say, "You've got inflammation." Instead, she might say that you have cardiovascular disease or inflammatory bowel disease or rheumatoid arthritis. That's because chronic inflammation "is a factor that's linked to the development or worsening of these—and numerous other—diseases and conditions," says Bennett. For instance, as many as 1 in 5 cancers is believed to be caused or influenced by inflammation, according to researchers in the department of biological engineering at the Massachusetts Institute of Technology in Cambridge. In fact, most acute and chronic diseases result from inflammation, noted a 2018 study in the journal *Frontiers in Medicine*. This means that conditions like Alzheimer's disease, obesity, heart disease, cancer, stroke, chronic respiratory diseases, asthma, allergies, chronic kidney disease, inflammatory bowel diseases, autoimmune diseases and more all fall into the giant bucket of chronic-inflammation-related disease. In addition, the aforementioned *Nature Medicine* study noted that mental health problems, including anxiety disorders, depression and schizophrenia are also associated with chronic inflammation.

"And then there's the issue of comorbidities," says Bennett, meaning that once you've got inflammation, there's a high probability of having another disease or condition. "When the body's normal functioning is disrupted in one area, it places stress on the functioning of other bodily systems." For example, people with inflammatory forms of arthritis, like

rheumatoid arthritis, are up to twice as likely to develop cardiovascular disease than those without.

Are We All Susceptible to Chronic Inflammation?

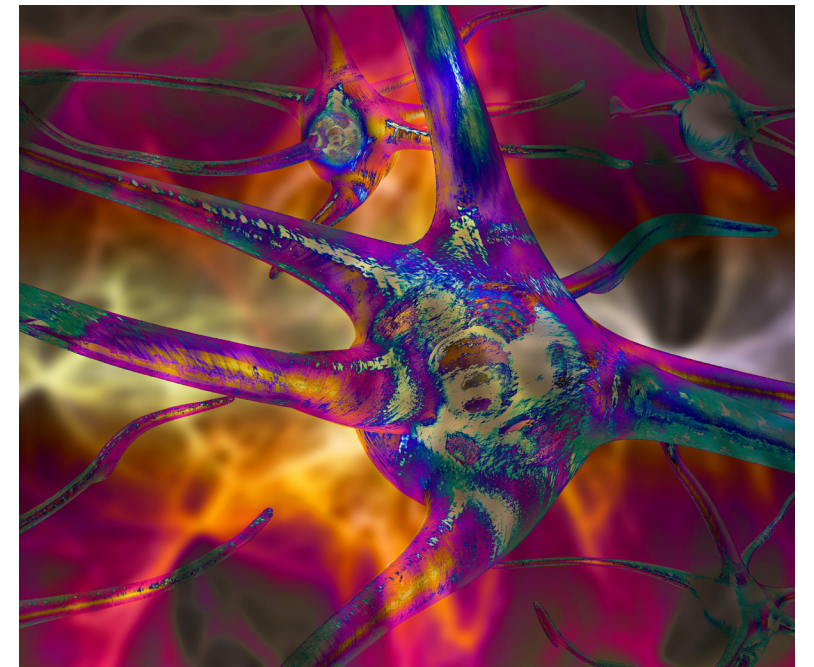
The short answer is yes. "Our bodies naturally shift toward an increase in inflammation with age," notes Elizabeth Bradley, M.D., medical director of Cleveland Clinic's Center for Functional Medicine. The longer we're on this earth, the more exposure we likely have to substances and situations that spur inflammation. In addition, gene regulation becomes impaired during the aging process, which tends to overactivate several key immune-to-brain communication factors. This, in turn, nudges the aging population into a more pro-inflammatory state, according to a 2019 report in the journal *Aging and Disease*. We also have a propensity toward weight gain with each passing year. "With that comes an increase in adipose tissue, which is inherently pro-inflammatory," says Dr. Bradley. (Adipose tissue, or body fat, is now well recognized as a major culprit in chronic inflammation, according to the *Aging and Disease* report.) That said, we are not all destined to face chronic inflammatory diseases. "I have patients in their 70s who feel great and are in

warmth and pain, which are signs that your body is fighting a bad guy and trying to protect you. The scab crusting over your cut? Inflammation. The egg on your forehead? Inflammation. That midwinter sore throat? You guessed it: inflammation. All these reactions quite literally "wall off your injury or infection to allow mobilized cells to foster healing," says Dr. Bykerk. Heck, prior to antibiotics, this natural process was all we had to aid our recovery.

When Inflammation Goes Awry

"The chemical messengers that communicate acute inflammation are no different than those that communicate chronic inflammation," says Jeanette Bennett, Ph.D., associate professor of

biological and health psychology at the University of North Carolina in Charlotte. "It's more about the amount of messengers sent and length of time they're activated." Helpful, acute inflammation is in and out, healing ouches, injuries and infections in about three to five days. With chronic inflammation, however, our well-oiled adaptive immune system misfires and our white blood cells (aka leukocytes) start to release large amounts of chemical messengers collectively called pro-inflammatory cytokines. These chemicals aggressively usher out "invaders" that aren't invaders at all. "With this misdirected attempt at repair and healing, our healthy tissue starts to break down," says Dr. Bykerk. This fruitless



good health because they have a healthy lifestyle—they eat well, they exercise—and they’re not doing anything to fuel the fire of inflammation,” says Dr. Bradley.

So What Causes the Initial Misfire?

There are multiple reasons why our body’s inflammatory response goes haywire. For instance, when an infection lingers in the body for an extended period, as in Lyme disease and hepatitis B or C, the immune system may continue to attack, sparking far more inflammation than is needed. “Things like toxin exposure, genetics and gene mutations also play a role in how or if chronic inflammation occurs,” says Dr. Bykerk. Meanwhile, some of the biggest drivers of chronic inflammation are things

like “stress, poor diet, lack of sleep, obesity, physical inactivity,” says Dr. Bradley. But it’s never just one thing. With inflammation, there’s always an interplay between factors like genetics, environment and diet. What triggers, say, your misfire is different from what may trigger another person’s. And predicting it isn’t easy. “We don’t know when exactly

the body goes from a healthy, well-regulated state to a pro-inflammatory state,” says Bennett. “Is it a slow progression, or does a switch get flipped? We don’t know yet.”

How Does Inflammation Decide Where to Attack?

How and where inflammation takes hold are not always intuitive. Depending on the individual, inflammation can strike in, say, your arteries, your joints, or the cells in your brain—almost anywhere—igniting any number of conditions. Sure, there are some instances when it’s easier to connect the dots than others. For instance, the chemicals that smokers inhale into the lungs may trigger inflammation that causes chronic obstructive pulmonary disease. “That’s a direct attack,” says Dr. Aggarwal. “Smoking directly affects inflammation in the lungs because those toxins are bad for that specific part

of the body.” But smoking-associated inflammation can cause damage throughout the body as well. For example, chemicals in cigarettes activate particular white blood cells called neutrophils that, in turn, release molecules that lead to increased inflammation, according to a 2016 report in the *Journal of Leukocyte Biology*. And those neutrophils are a vital factor in the development of atherosclerosis, which is plaque buildup on artery walls.

Will the inflammatory response set off by cigarettes have the same impact on all who smoke? No. “Our genetics greatly influence how exactly inflammation will affect our health,” says Elizabeth W. Boham, M.D., R.D., medical director of the UltraWellness Center in Lenox, Massachusetts. For instance, if you’re genetically predisposed to, say Crohn’s disease, your trigger, whatever that is, will activate the gene response to Crohn’s. “At least that’s what we think happens,” says Dr. Aggarwal, who’s own chronic inflammatory condition, rheumatoid arthritis, didn’t surface until the mental and physical stress of having her third child provoked it.

What Are the Signs of Chronic Inflammation?

Here’s the kicker: “There are no classic signs of early chronic inflammation,” says Dr. Bykerk. The symptoms are, well, vague. Think body aches, fatigue, changes in mood, brain fog, constipation, heartburn, weight gain. “I have patients in their 40s and 50s who say things like, ‘I ache because I’m old,’ and I’m like, ‘No, that’s not it!’ They have no idea that they’re inflamed,” says Dr. Bradley. “They don’t realize that they shouldn’t ache at all.” Instead, people often learn something is amiss only after they’re diagnosed with a chronic-inflammation-related condition.

There are tests that you can take, but they may not be as helpful as you’d think. “We use high-sensitivity CRP [C-reactive protein] testing with cardiovascular disease and CRP testing with autoimmune diseases to measure inflammatory markers,” says Dr. Aggarwal. “In these situations, we have the data to support their use.” For instance, there are specific levels of CRP that correspond to heart disease risk. You’re at low risk of developing cardiovascular disease if your hs-CRP level is below 1.0 mg/L. You’re at high risk if your level is

People often learn something is amiss only after they’re diagnosed with a chronic-inflammation-related condition.

+
IT IS RECOMMENDED THAT ADULTS GET AT LEAST 150 MINUTES OF MODERATE-INTENSITY EXERCISE A WEEK.





YOGA CAN HELP REDUCE STRESS BY REGULATING THE NERVOUS SYSTEM.

above 3.0 mg/L. “But there’s not enough data yet to support the use of this test in other areas,” says Dr. Aggarwal, noting that there’s far too much variability in CRP levels to make the test useful as a general screen. “Consider it this way,” she says. “The test is just one marker. You may have totally normal CRP but have another inflammatory marker that we just haven’t learned about yet.” Or your CRP may be high because you’ve got a respiratory infection or gingivitis, which temporarily bolsters your numbers. “Ultimately, it’s always better to fall back on risk factors to see if you have a higher chance for inflammation,” says Dr. Aggarwal.

Before diving into what habits are putting you at risk, it’s smart to first look at balance. “Think about it as what you give your body versus what you take from your body,” says Dr. Aggarwal. “Say you

have poor sleep habits, you’re sedentary, and you smoke. Those are all stressors on your body.” Compare your personal stressors to what you offer your body as resources, such as practicing yoga and eating healthy. “If there’s an imbalance between what you take and what you give, that can trigger inflammation,” she says.

Excess weight is a major driving factor for chronic inflammation. “Over 40% of Americans are overweight or obese, and about that same amount are chronically inflamed,” says Dr. Bradley. “There’s a reason for that.” Adipose tissue releases inflammatory chemicals, and it reduces the production of adiponectin, a protein that has anti-inflammatory properties. (While excess weight drives inflammation, inflammation also drives weight gain, making this an especially vicious cycle, according to a

2019 study in the journal *Metabolism Open*.) Overall obesity can trigger inflammation, but belly fat is notably dangerous on its own, predisposing folks to the likes of heart disease, type 2 diabetes, insulin resistance and more. A 2020 report in the *Journal of Clinical Investigation* even connected belly fat to Alzheimer’s disease; it noted that this type of fat overactivates microglia, which are immune cells in the brain, increasing brain inflammation and one’s risk for Alzheimer’s.

Chronic stress, no matter where it is coming from, is stress that occurs every day, all day, for many weeks or maybe months or years. With it, the so-called stress hormone cortisol is present at high levels for an extended period, which the body will begin to perceive as a threat. “What ends up happening is immune cells start to become activated, and once they are activated, there’s very little opportunity to turn it down,” says Bennett, who notes that chronic stress and its effects vary from person to person. “Your personal ramifications are linked to your coping skills, resources and ability to adapt.”

When you’re working on a sleep deficit, the hormone cortisol breaks down more slowly. “Therefore, when we don’t sleep, cortisol remains at a higher level. And high levels of cortisol over time lead to inflammation,” says Dr. Aggarwal. To wit: people who experience poor sleep quality or insomnia have increased levels of pro-inflammatory markers in their systems, according to a 2016 meta-analysis featured in the journal *Biological Psychiatry*.

What you eat also has a huge impact when it comes to chronic inflammation. Typical pro-inflammatory foods include red and processed meats; refined carbohydrates, such as white bread and packaged snacks; fried food; and sugar-sweetened beverages. “Some of these foods result in a change in blood sugar, which leads to inflammation. Other foods drive inflammation based on a shift in the microbiome,” says Dr. Boham. Regardless of the hows and whys, consuming

a pro-inflammatory diet is linked to higher circulating pro-inflammatory chemicals and lower anti-inflammatory chemicals. And the results can be dangerous. For example, a recent large-scale, long-term study in the *Journal of the American College of Cardiology* found that folks who consumed the most pro-inflammatory diets had a 38% increased risk of developing cardiovascular disease compared with those who had the most anti-inflammatory diets. And it’s not just about poor diets leading to more pounds: a 2018 study in *JAMA Oncology* found that a pro-inflammatory diet increases one’s risk for colorectal cancer, even in lean women.

“Right now, almost half of our society is chronically inflamed—and it’s happening earlier and earlier,” says Dr. Bradley. But there’s a lot of hope. “People can 100% bring down chronic inflammation,” says Dr. Aggarwal. “I did.”

For seven years, Dr. Aggarwal has been off medications for her rheumatoid arthritis, thanks to things like tweaking her diet and finally finding time for herself. “I can’t change my genes, but I can change how my body expresses and responds to those genes,” she says. “Today, my inflammatory markers are totally flat. I took the time to heal my body, and I’m doing so much better. Other people are getting better too. It’s possible.” ●

