

The enemy within

Inflammation is the hidden culprit behind dozens of health problems.

Here's what you need to know about it—and the new science on how best to keep it in check.

WHEN IT FUNCTIONS PROPERLY, inflammation is a quick, natural response designed to help the body heal. When it doesn't, it simmers at chronic levels, which in recent years have been linked to a wide range of ills, including dementia, heart disease, asthma, migraines, colitis, cancer, diabetes, and depression. In fact, chronic inflammation has been connected with the development of at least half the diseases on the Centers for Disease Control and Prevention's top-10 causes of mortality. It's this sinister pervasiveness that has given inflammation a nega-

tive reputation and made it a health buzzword—inspiring books, diets, and supplements, as well as serious medical research. While scientists are actively studying exactly why chronic (or systemic) inflammation occurs, what damage it can cause, and how we can reverse it, there's much we already know about this bodily response gone awry.

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Your defense system in overdrive

Here's how inflammation is supposed to work: When the body senses that something is wrong, due to injury or infection, it sends white blood cells and inflammatory cytokines, like C-reactive protein (CRP) and interleukin-6 (IL-6), to the area, to help repair the damage or fight off the invader. Certain pro-inflammatory enzymes, such as COX-2, produce prostaglandins on-site. This rapid, multipronged response usually generates a hot or inflamed feeling in the affected part of the body, giving inflammation its name.

"Ideally we want inflammation to come in, hit hard, and go away," says Christine McDonald, Ph.D., a member of the pathobiology department at the Cleveland Clinic Lerner Research Institute. But when those inflammatory chemicals are released on a continuous basis, without any injury or infection to confront, they go from healing damaged cells to harming healthy ones. "When it doesn't turn off, you get chronic, smoldering inflammation that can eventually cause tissue and cell damage," says McDonald.

Although there is no definitive answer as to why inflammation sometimes goes haywire, researchers have identified a number of different factors that create chronic inflammation.

A MALFUNCTIONING PROTEIN.

In one recent study, researchers at Georgia State University's Institute for Biomedical Sciences, in Atlanta, found that a protein called CYLD plays a critical role in controlling the inflammatory response to pathogens

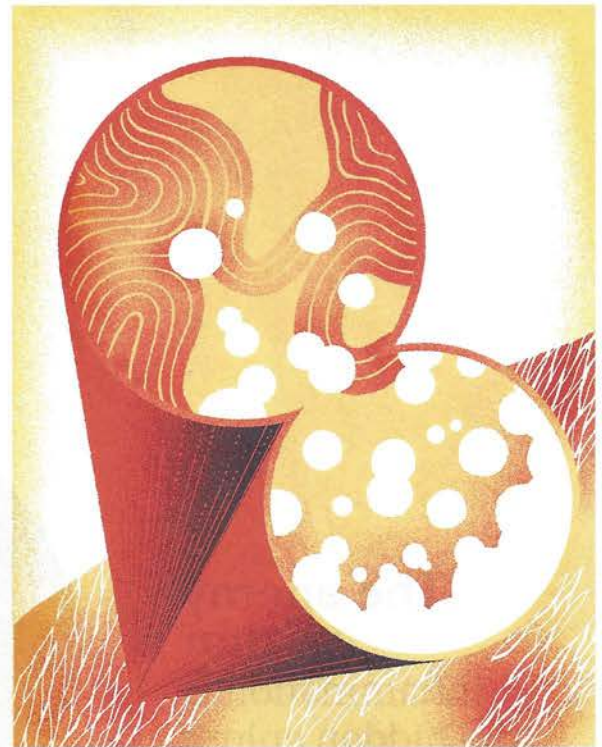
(such as viruses and bacteria). "It acts like a brake pedal to turn off that defense," says lead author Jian-Dong Li, M.D., Ph.D. "Uncontrolled, overactive inflammatory response could likely be due to some defect in this brake pedal."

YOUR BODY'S RESPONSE.

Ironically, you could end up with lingering, out-of-control inflammation because your body's normal inflammatory response in the face of infection is subpar. "The body gets the signal to launch an inflammatory response to get rid of the bacteria, but it doesn't do the whole job. A few bacteria hang out, grow, and trigger a bigger response," explains McDonald. "Your cells keep giving off the distress signal, which continues to generate inflammation without ever totally getting rid of the bacteria that's triggering it."

EXCESS WEIGHT. "Excess adipose, or fatty, tissue generates inflammatory cytokines," says Catherine Duggan, Ph.D., a principal staff scientist at the Fred Hutchinson Cancer Research Center, in Seattle. "So being overweight can mean your body is in a state of long-term, low-grade inflammation."

PERSONALITY TRAITS. Are you the conscientious type? Then chances are you have lower levels of inflammation than someone less diligent. Study participants who were least conscientious had a nearly 50 percent increased risk of high CRP levels than did those ranked most conscientious, in a 2014 study published in the journal *Psychoneuroendocrinology*. "Those less conscientious are more likely to smoke, exercise less, and eat less healthy food," says Angelina Sutin, Ph.D., one of the study's coauthors and an assistant professor at the Florida State University College of Medicine, in Tallahassee. "The trait is also associated with greater



stress-related activation of the hypothalamic-pituitary-adrenal axis, along with excess body weight—both of which contribute to inflammation." Another study links being open to new experiences with lower levels of inflammation. Although you can't necessarily change your personality, you can assiduously strive to be open to new things.

YOUR MOOD. More and more research is connecting stress to the body's immune response and chronic inflammation. "Chronic stress changes gene activity of immune cells before they enter the bloodstream," says Victoria Maizes, M.D., the executive director of the University of Arizona Center for Integrative Medicine, in Tucson. They think they're going in to fight an infection, and even if there isn't one, they help spur inflammation.

What's more, a recent review from Rice University found a surprisingly strong link between stress, higher inflammation levels, and depression. In patients suffering from clinical depression, levels of CRP and IL-6 were up 50 percent.

YOUR GUT. About 70 percent of your immune system operates out of your gut, so it's no surprise that an imbalance in gut bacteria can impact the health of the rest of your body. If your gut's microbiome is off, the resulting inflammation can help fuel conditions such as irritable bowel syndrome and colon cancer, as well as conditions outside the digestive system. "Problems with the microbiome can contribute to inflammatory conditions such as arthritis, depression, and neurological disease," says Eamonn Quigley, M.D., the section chief of gastroenterology at Houston Methodist Hospital.

EXPOSURE TO AIR POLLUTION. We already know that cigarette smoke contains toxins that stimulate an inflammatory response in the body. Now research has also found an association between greater exposure to air pollution and higher levels of inflammation-related substances, such as CRP and IL-6.

Feeling the heat

Inflammation isn't always obvious. Swelling and joint pain are clear signs of systemic inflammation, but other signs include gum disease, unexplained rashes, fatigue, headaches, and muscle stiffness. Worse, chronic inflammation is often invisible until an illness such as heart disease or diabetes—or an autoimmune condition, like rheumatoid arthritis—is diagnosed.

Your doctor might not be looking for inflammation, so keep your own

checklist if you notice any symptoms on a regular basis. A simple blood test can reveal substances that doctors use as markers of inflammation (such as CRP and IL-6), but unless you have specific symptoms, the tests aren't always enlightening. "High CRP is a general sign that something is amiss," says Maizes, "but it doesn't point you to a specific disease." That said, based on findings from a large clinical trial in 2009, many doctors now recommend testing CRP for women over 60 and men over 50 because of the strong connection between inflammation and coronary disease, even in patients with normal cholesterol and an average risk of heart disease. "A large number of patients with normal cholesterol had high CRP, and when treated with statins, they had a 44 percent

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lower risk of suffering a major heart event," says Nieca Goldberg, M.D., the medical director of the NYU Langone Joan H. Tisch Center for Women's Health, in New York City.

How to quell inflammation

The standard approaches for calming chronic inflammation include non-steroidal anti-inflammatory (NSAID) drugs, like ibuprofen, and other medications, along with lifestyle behaviors. These include eating salmon, mackerel, and other fish high in omega-3 fatty acids, drinking flavonoid-rich tea, and getting adequate sleep and exercise. Now new research reveals more ways to keep inflammation at bay. Although none have yet been proven to completely eliminate your risk of health conditions like heart disease and dementia, all are beneficial strategies that will probably improve your health.

LOSE A FEW POUNDS, AND TAKE VITAMIN D. Losing as little as two pounds can decrease adipose tissue enough to affect levels of inflammatory markers. And increasing your vitamin D intake can help even more. In a recent study published in *Cancer Prevention Research*, overweight women who had lower-than-recommended vitamin D levels and then lost 5 to 10 percent of their body weight and supplemented with 2,000 international units (IU) of vitamin D



daily saw a 37 percent higher reduction in the inflammatory cytokine IL-6 than did those who lost weight without taking vitamin D.

BE SOCIAL. Loneliness causes chemical reactions that can contribute to cellular inflammation—which can increase the odds of related illnesses, including cancer and diabetes—according to a recent study from the University of Chicago. Researchers tracking 141 people over five years found that when people felt lonely, levels of norepinephrine (a fight-or-flight hormone) surged, increasing the activity of inflammatory genes. “It’s as if loneliness is interpreted by the body as a threat,” says Steve Cole, Ph.D., a professor of medicine at UCLA and the lead author of the study. The study found that loneliness predicted inflammation even a year later, and inflammation also predicted loneliness. “They may help propagate one another in a vicious cycle,” says Cole.

SPICE THINGS UP. Consuming a teaspoon or less of turmeric daily can reduce oxidative stress associated with inflammation, according to Chris D’Adamo, Ph.D., the director of research at the Center for Integrative Medicine at the University of Maryland School of Medicine, in Baltimore. D’Adamo also recommends ginger, which inhibits COX-2 and prostaglandins from being produced, and cayenne pepper.

POP A PROBIOTIC. Adults with inflammatory conditions (including psoriasis, chronic fatigue syndrome, and ulcerative colitis) who took a probiotic supplement for eight weeks had lower levels of inflammation compared with people who took a placebo, according to a 2013

study from University College Cork, in Ireland. “Even in healthy subjects, we saw a significant shift in an anti-inflammatory direction,” says Quigley, who was on the research team. He and his colleagues found that introducing the healthy bacteria *Bifidobacterium infantis* 35624 into the gut can improve immune functioning and reduce inflammation.

MAKE IT A VEGGIE BURGER. Not only the amount but also the type of protein that you’re eating can affect your inflammation levels. Lower protein intake overall was associated with lower levels of inflammatory markers in a 2014 study published in the journal *Nutrition*. And when the intake was categorized, greater red and white meat consumption—no matter the overall amount—was linked to higher levels of inflammatory markers than was the consumption of plant proteins.

CURB YOUR OMEGA-6 INTAKE. Consuming moderate to high amounts of omega-6 fatty acids—found in corn, soybean, and grapeseed oils, for example—can promote inflammation and increase your risk of heart disease. “Omega-6 initiates inflammatory processes, and omega-3 terminates them,” says D’Adamo. But it’s more complicated than just omega-6 = bad; omega-3 = good. The ratio between the two matters. “Most Americans are getting 20 to 1, when ideally it should be more in the range of 3 to 1,” says D’Adamo.

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