

What autoimmune diseases are and what can be done to alleviate them

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If you have celiac disease, inadvertently consuming even a single crumb of bread can lead to gastrointestinal upset for weeks or months. For those who suffer from lupus, a flare can damage kidneys—or even

worse. People with rheumatoid arthritis suffer from debilitating joint pain.

They are very different ailments, but all have one thing in common: They are autoimmune diseases, conditions that arise when the body's immune system attacks not external pathogens but the body itself.

Increasingly, researchers are finding other diseases that have a root cause in autoimmune function. Some 24 million Americans are affected by more than 80 autoimmune diseases, according to the National Institute of Environmental Health Sciences, and it seems as if more people are being diagnosed with them than before.

Normally, when our bodies are faced with pathogens—such as bacteria or viruses—our immune systems kick into high gear to protect us from these invaders. But sometimes our immune systems confuse parts of our tissues and organs as foreign invaders and attack them instead. The [inflammatory response](#) that can knock out an invading bacterium ends up damaging our own health.

Pilar Alcaide, a Kenneth and JoAnn G. Wellner Professor at Tufts University School of Medicine, is an immunologist, focusing on how the immune system impacts cardiovascular health. She also has a personal understanding of these types of diseases. When she was around 6 years old, she was diagnosed with the skin condition psoriasis—an autoimmune disease. It was unusual for a young person to experience the severe psoriasis type she was diagnosed with, and a reminder that these diseases affect all kinds of people.

Alcaide explains more about autoimmune diseases, what causes them, who gets them the most, and what can be done about them.

Do scientists know why this autoimmune response

happens?

There are many different types of autoimmune diseases. A classic one is when there is a mutation on a gene—such as the one that causes Type 1 diabetes. People who have that mutation, their pancreas is attacked by the immune system, with the result that insulin production stops.

Typically autoimmune diseases that are determined by just one gene are developed from birth or from a young age. But for many other autoimmune diseases, genetics is only one part of the cause. For instance, I had severe psoriasis as a child, but most people have mild, moderate, or severe forms of the disease later in life, so it is thought that environment plays a strong role in its development.

In many cases, autoimmune diseases develop with age over time, meaning it's often a combination of genetics, environment, and physiological and mental stress. There's a lot of research demonstrating that the level of stress plays an important role—the environment and stress.

A lot of these autoimmune diseases have flares, when your immune system—for whatever reason—is responding more aggressively than normal.

How does the immune system work normally?

Say a virus or a pathogen hits you. Your body realizes there is a pathogen, and the immune system starts releasing proteins called [cytokines](#). Some of these cytokines will induce fever, which is good—a lot of viruses die at high temperatures. A fever also tells your body that you cannot fight the infection without other internal help.

Then other cells called [lymphocytes](#) come to help kill the infection. Pro-inflammatory lymphocytes are specialized, and typically they go to where the [trigger](#) was.

But then your body needs to turn off the response. When the pro-inflammatory lymphocytes have done their job, anti-inflammatory lymphocytes arrive and suppress the response.

What happens when it goes haywire in an autoimmune response?

The first barrier of protection to self—our tissues and organs—is what we call immune tolerance. That's when anti-inflammatory cells recognize, say, "This is a skin protein. It's okay. You don't need to respond to that." That's homeostasis—the body at equilibrium.

But in some cases, a genetic mutation causes a protein to appear that is very similar to something that is part of us, but not quite. Then the inflammatory cells recognize it as a foreign thing, as if it were a pathogen, and they start inflammation.

If you are infected with something, you need inflammation, and when you clear that infection, you need anti-inflammation. With autoimmunity diseases, if you skip this tolerance phase, inflammation develops.

The skin, for example, closely interacts with nerves and both produce substances that act on each other's receptors. For example, [neuropeptides](#) can alter immune cells in the skin that produce cytokines and trigger an inflammatory response.

Can you talk about some of the environmental factors that researchers have found?

Most of the research that has been done is around environmental toxins that come from smoke or air pollution in large cities. Those toxins break up into small molecules, and certain immune cells have receptors for those small molecules.

That triggers the activity of these immune cells, which release cytokines that induce inflammation wherever they are. Nutrition is also key—some foods induce inflammation, while other healthy foods don't.

Why does the autoimmune response happen in some people versus others?

There are a lot of risk factors. One is genetics. You can have a genetic mutation that triggers a response.

You could also have hidden mutations or hidden factors that are normally silent—you don't realize that there's this constant battle of anti- or pro-inflammation inside you, because it's hidden.

But then something happens, like an environmental trigger, such as a hydrocarbon—the chief component of oil and natural gas, for example—that activates receptors that your immune cells express. Then they will become pro-inflammatory, and then you have autoimmunity.

Another trigger involves the microbiota—the microorganisms in our intestines. Your gut is the reservoir for immune cells—you have tons of bacteria in your gut and your immune cells live with them. They're the so-called good bacteria.

But then you eat something that somehow disrupts that, and all of a sudden, your immune cells start recognizing the bacteria as foreign. That happens, for instance, in Crohn's disease and ulcerative colitis, though

those diseases aren't exclusively triggered that way.

Is the incidence of autoimmune disease increasing? And if so, is it because people are recognizing it more, or is it because there is more overall?

That's a tough one. Autoimmune diseases have always been diagnosed, but maybe now there's more diagnosis—perhaps because more people go more often to the doctor.

But it's clear that lifestyles have changed—working hard, not taking time for yourself, more stress, unhealthy fast food, more pollution—that definitely doesn't help. And the environment is presenting more triggers.

Do women get autoimmune diseases more than men?

Yes, with a few exceptions. Typically, more women than men get autoimmune diseases. But when men get it, it is way more severe than for women.

That's true, for example, with lupus, which women are 10 times more likely to get than men. Lupus is a very complex autoimmune disease, and an example of one influenced by several genetic and environmental factors. You have a variety of immune responses happening, including damage to many organs. It starts in the skin, but then it can go to your kidneys. It's massive.

But when a man gets it, it's way more severe, with kidney damage, especially African American men. They have the worst prognosis of all with lupus.

What are treatments for autoimmune diseases?

Because this is a pro-inflammatory condition, people try to dampen inflammation with [steroids](#). Methotrexate was one example, and cyclosporine and many other drugs—those are broad anti-inflammatory drugs.

The issue is that you cannot take them forever, because you suppress everything. So, you could use them in case of flares. But with either topical or systemic corticosteroids, the minute you stop taking them, the inflammation comes back.

In the past decade or so, as researchers started understanding the individual roles of specific immune cell subsets, and the cytokines they make, it became very clear that in most autoimmune diseases, the early players that are super-inflammatory are specific cells, and they've developed blocking antibodies towards those.

Now those are very commonly used. They're called biologicals, because unlike the global immunosuppressors, they recognize cytokines that our own body makes.

Do the biologicals used in treatment for autoimmune disease have downsides?

Yes, they do. One is that because of their immunosuppressive nature, sometimes when you take them for too long, some lymphomas form—cancer of the lymph nodes—because lymphoid tissue is where immune cells divide. They also have other side effects such as higher risk of infections.

I think that developing the biologicals was one of the biggest breakthroughs in medicine, because there were people, especially with arthritis and psoriatic arthritis, who couldn't really live a normal life until

these treatments became available.

The gold standard would be to find something that is more tissue specific, that you wouldn't dampen inflammation systemically. But for some autoimmune diseases, you need to dampen it systemically as well.

Are there other treatments?

Yes. For skin disorders, phototherapy is something that works very well. A certain wavelength of light, mimicking that of the sun, suppresses inflammation. That's a very non-invasive treatment that suppresses [inflammation](#) in your skin.

Phototherapy with natural or artificial light is used in vitiligo, which is an autoimmune disorder where people get depigmentation of the skin. It also works very well in certain types of psoriasis.

Researchers are also trying to develop a vaccine for psoriasis. I was in a trial when I was a kid, but unfortunately it didn't work—more work understanding of the drivers of autoimmunity need to be done by immunologists.

Are autoimmune diseases more common in higher income countries vs. poorer countries?

It's hard to tell, because a lot of people in poor countries are not diagnosed. Some autoimmune diseases are related to ethnicity. For instance, autoimmune skin disease like vitiligo and psoriasis are prevalent in the Middle East. Some autoimmune diseases are not so easy to diagnose, but in the skin it's so easy to see.

That's the difference versus something like Crohn's disease—many

people in poorer countries don't know they have it, because even if their stomach hurts or they bleed, they may think it's a parasite.

I think certain autoimmune diseases are definitely diagnosed more in the U.S. That might have to do with the lifestyle as well, but also because of the ability to diagnose it.

Are autoimmune diseases more difficult to diagnose than other diseases?

I think they're difficult to diagnose because if it's systemic, there are a lot of cross relations between that and other diseases.

So, let's say that you develop a rash, and you don't think it's autoimmunity. But then the rash is on your face and spreads. If you also had a lot of pain in your kidneys, then it could be lupus.

And there are people who present with more than one autoimmune disease. People with psoriasis very often develop rheumatoid arthritis. And people with Crohn's disease often develop that as well.

Rheumatoid arthritis is one of the most prevalent [autoimmune diseases](#). It's different from osteoarthritis, which is triggered by mechanical stress in the joints. People who have psoriasis in the joints often develop psoriatic arthritis—very much like rheumatoid arthritis.

There are just so many different autoimmune diseases—more than are probably realized.

That's why it's critical to learn as much as we can about the immune system, how it works in normal conditions, and how it reacts to different insults, so we can investigate how to modulate it, dampening or

enhancing its response when needed to treat autoimmunity.

Most of the diseases that kill the majority of the people are somehow immune-related, so understanding immunity will help prevent and treat not only autoimmunity but also other chronic inflammatory diseases.

Provided by Tufts University

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