

Your Immune System and Auto Immune Disease

Scientists who study the immune system say chance mutations, coupled with a viral infection, can trigger autoimmune reactions that create a potentially deadly family feud within your body.

The finding, which appears in the current issue of the *Journal of Experimental Medicine*, is preliminary and unlikely to produce any help for patients in the near future. However, researchers say, it could one day lead to treatments for lupus, rheumatoid arthritis and early-onset, or Type I, diabetes. Together, autoimmune diseases are among the top 10 killers of women in America.

A prime example of the link is rheumatic heart disease, an autoimmune attack on heart tissue that's thought to result from repeated strep infections during childhood.

The latest study offers at least one explanation of how your immune system can turn into your worst enemy.

The research, led by Andrew Caton, of the Wistar Institute in Philadelphia, hinges on a class of immune agents called memory B cells. They are the first dominoes in the cascade of reactions that make up an immune response, and they have two key jobs.

The first is to recognize an invading organism, such as a virus, and warn other immune cells of its presence. They do this by generating proteins, called antibodies, which are specific to the microbe. They can also neutralize the invader by attaching themselves to it. B cells "help keep you from dying" within days from the initial infection, says Caton.

But there's a subset of B cells that, when they meet an invader, don't do anything immediately. Instead, they retreat to the spleen, and with the help of other immune cells, they begin to mutate randomly and with remarkable haste, he explains.

In clusters known as germinal centers, they refine themselves into highly specific cells that flood the bloodstream and defeat the infection. This process, which occurs about a week after initial infection, also gives the body a "memory" of the invader, Caton says. That helps them fight off subsequent attacks from the same organism.

It's also the reason vaccines work, since these B cells live a long time and "do a better job of recognizing the virus than the ones you have inherited," he says.

In the latest study, Caton and his colleagues showed that, during their time in the spleen, these B cells can mutate and become hostile to your body. Using a strain of mice genetically modified to express an influenza protein, hemagglutinin, they were able to disguise the viral protein as part of the body.

The modified mice appeared to be healthy. But when they infected the animals with flu, their immune cells launched a muted attack against the transferred protein.

Since B cells in the first wave of attack die off, the autoimmune reaction had to originate with the B cells produced in the second phase, Caton says.

In other words, the combination of random mutations with a viral invasion sparked an autoimmune response, albeit a mild one, he says.

What's not clear is why autoimmune reactions choose to pick on particular tissues, like the joints in arthritis or pancreas in diabetes.

"What makes it harmful rather than benign is similar to saying, 'Why are some cell masses benign and others malignant?'" Caton says. "How that decision is made is a big mystery."

If infections do indeed spark autoimmune reactions, then vaccination would be the obvious answer.

Yet Rose says at least one other new study seems to show the incidence of autoimmune disease rises with more immunization.

