

# Depression, aging, and proteins made by a virus may all play role in heart disease

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Researchers here have linked an increase in two immune system proteins essential for inflammation to a latent viral infection and proposed a chain of events that might accelerate cardiovascular disease. The same process may be involved in a host of other ailments plaguing the elderly.

The findings also suggest that chronic depression may play a key role in starting the cascade that can lead to the buildup of plaques clogging coronary arteries.

The researchers' report, their latest in a nearly three-decade-long effort to understand the role psychological stress plays in weakening the immune system, was published in the journal *Brain, Behavior and Immunity*.

Ronald Glaser, a professor of molecular virology, immunology and medical genetics at Ohio State University, said, "To me, this suggests a new way of thinking about how these diseases develop. We carry around these latent herpes viruses in our bodies virtually all our lives and periodically they can hurt us, inducing biological events that could lead to an increased risk of atherosclerosis."

Glaser, head of Ohio State's Institute for Behavioral Medicine Research, has focused for years on Epstein-Barr virus (EBV), one of eight different herpesviruses that can remain dormant in the body for a lifetime.

“Perhaps more than 90 percent of the people in North America have been infected by EBV by the time they're adults,” Glaser said. “Virtually everybody in the country is carrying this virus.”

Glaser, James Waldman, an associate professor of pathology, Marshall Williams, a professor of molecular virology, immunology and medical genetics, and Janice Kiecolt-Glaser, a professor of psychiatry and psychology, initially focused on the role that two essential proteins – interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a) -- play in producing inflammation, a major part of the body's immune response.

As the immune system ages, the levels of IL-6 in the body increase in the blood. Some of that IL-6 is created by immune cells called macrophages that rush to the site of an infection or injury. Earlier work by the team also showed that increases in psychological stress and depression can substantially raise the levels of IL-6 and TNF-a in the body.

Increased stress and depression can also trigger the latent virus to reactivate and begin reproducing inside cells

The researchers also knew that as Epstein-Barr virus begins to multiply in cells in the body, it produces a protein called dUTpase that, in turn, can stimulate macrophages to make even more IL-6.

“The more IL-6 levels rise in the body, the greater a person's risk is for disease,” Glaser said, adding that IL-6 increases, as well as depression, have been associated with cardiovascular disease, osteoporosis and type-2 diabetes.

The researchers developed a model to test these linkages by using endothelial cells that line the inside of veins in umbilical cord tissue. They wanted to see how the cells themselves, as well as the immune macrophages, reacted when exposed to the virus as well as the dUTpase

protein.

In those experiments, the production of IL-6, as well as TNF-a, were increased just as they would be as part of the inflammatory process in the body. Such chronic incidents of inflammation are integral to the onset of atherosclerosis, Waldman said, as well as other diseases.

“Basically, we're seeing all of these factors as playing a significant role in the production of these proinflammatory proteins,” he said. “We were very surprised to find all these connections. They weren't expected.

“This may help us understand just how atherosclerotic disease may occur, or how it is exacerbated by many factors.”

The researchers point to one value of their findings:

“People need to remember how important depression is, and that when they're depressed, it can reactivate these viruses, starting the cascade that leads to inflammation, perhaps increasing the risk of cardiovascular disease,” according to Glaser.

“So treating depression is very important,” he said.

Source: Ohio State University

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