Understanding the links between inflammation and chronic disease

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American parents may want to think again about how much they want to protect their children from everyday germs.

A new Northwestern University study done in lowland Ecuador remarkably finds no evidence of chronic low-grade inflammation -- associated with diseases of aging like cardiovascular disease, diabetes and dementia.

In contrast, about one-third of adults in the United States have chronically elevated C-reactive protein (CRP). Acute elevations in CRP -- a protein in the blood whose levels rise as part of the inflammatory response -- are important for protecting us against infectious disease. But when CRP is chronically produced, it is associated with chronic diseases.

"In other words, CRP goes up when you need it, but it is almost undetectable when you don't, after the infection resolves," said Thomas W. McDade, professor of anthropology at Northwestern and faculty fellow at the university's Institute for Policy Research. "This is a pretty remarkable finding, and very different from prior research in the U.S., where lots of people tend to have chronically elevated CRP, probably putting them at higher risk for chronic disease."

McDade said the findings build on his previous research in the Philippines, which found that higher levels of microbial exposure in infancy were associated with lower CRP as an adult. Similar exposures during infancy in lowland Ecuador, where rates of infectious disease

continue to be high, may have a lasting effect on the pattern of inflammation in adulthood.

"In my mind the study underscores the value of an ecological approach to research on the immune system, and it may have significant implications for our understanding of the links between inflammation and chronic disease," McDade said. "This may be particularly important since nearly three-quarters of all deaths due to cardiovascular disease globally now occur in low- and middle-income nations like the Philippines and Ecuador."

The new research, which was conducted as part of the Shuar Health and Life History Project (http://www.bonesandbehavior.org/shuar/), suggests that higher levels of exposure to infectious microbes early in life may change how we regulate inflammation as adults in ways that prevent chronic inflammation from emerging. Infectious microbes have been part of the human ecology for millennia, and it is only recently that more hygienic environments in affluent industrialized settings have substantially reduced the level and diversity of exposure.

A growing body of research has shown that higher levels of chronic inflammation are associated with diseases of aging like cardiovascular disease, diabetes and dementia. But current research is based almost exclusively on people living in affluent industrialized countries like the United States.

"We simply do not know what chronic inflammation looks like in places like the Ecuadorian Amazon and other parts of the world where infectious diseases are more common," McDade said.

As a result, McDade, director of the Lab for Human Biology Research and director of Cells to Society (C2S): The Center on Social Disparities and Health, and collaborators at the University of Oregon set out to

investigate what factors in the environment and during development influence how people regulate inflammation as adults. The study was conducted in lowland Ecuador – in a group of 52 adults between the ages of 18 and 49.

Based on current clinical criteria, McDade and colleagues did not find a single case of chronic low-grade inflammation among adults living in the Ecuadorian Amazon. McDade said people in these places are still dying of diseases such as cardiovascular disease, but probably not through processes that involve inflammation.

In terms of population health, McDade said these findings suggest that the association between inflammation and cardiovascular disease frequently reported in the United States may only apply in ecological settings characterized by low levels of exposure to infectious disease.

"It builds on research on chronic inflammation and cardiovascular disease in the U.S. and other affluent, industrialized settings and suggests that patterns seen here may not apply globally," McDade said. "It also suggests that the levels of chronic inflammation we see in the U.S. are not universal, and may be a product of epidemiological transitions that have lowered our level of exposure to infectious microbes."

More information: "Analysis of Variability of High Sensitivity C-Reactive Protein in Lowland Ecuador Reveals No Evidence of Chronic Low-Grade Inflammation" is currently available online in the Early View section of the *American Journal of Human Biology* (onlinelibrary.wiley.com/journal/10.1002/%28ISSN%291520-6300/earlyview).

Provided by Northwestern University

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