Common virus could cause high blood pressure

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Researcher Clyde Crumpacker in his laboratory at Beth Israel Deaconess Medical Center.

(PhysOrg.com) -- A new study suggests for the first time that cytomegalovirus (CMV), a common viral infection affecting between 60 and 99 percent of adults worldwide, is a cause of high blood pressure, a leading risk factor for heart disease, stroke and kidney disease.

Led by researchers at Beth Israel Deaconess Medical Center (BIDMC) and published in the May 15, 2009 issue of PLoS Pathogens, the findings further demonstrate that, when coupled with other risk factors for heart disease, the virus can lead to the development of atherosclerosis, or hardening of the arteries.

"CMV infects humans all over the world," explains co-senior author

Clyde Crumpacker, MD, an investigator in the Division of Infectious Diseases at BIDMC and Professor of Medicine at Harvard Medical School. "This new discovery may eventually provide doctors with a whole new approach to treating hypertension, with anti-viral therapies or vaccines becoming part of the prescription."

A member of the herpes virus family, CMV affects all age groups and is the source of congenital infection, mononucleosis, and severe infection in transplant patients. By the age of 40, most adults will have contracted the virus, though many will never exhibit symptoms. Once it has entered the body, CMV is usually there to stay, remaining latent until the immune system is compromised, when it then reemerges.

Previous epidemiological studies had determined that the CMV virus was linked to restenosis in cardiac transplant patients, a situation in which the heart's arteries "reblock." The virus had also been linked to the development of atherosclerosis, the hardening of the heart's arteries. But, in both cases, the mechanism behind these developments remained a mystery. This new study brought together a team of researchers from a variety of disciplines - infectious diseases, cardiology, allergy and pathology - to look more closely at the issue.

"By combining the insights of investigators from different medical disciplines, we were able to measure effects of a viral infection that may have been previously overlooked," explains Crumpacker.

In the first portion of the study, the scientists examined four groups of laboratory mice. Two groups of animals were fed a standard diet and two groups were fed a high cholesterol diet. After a period of four weeks, one standard diet mouse group and one high-cholesterol diet mouse group were infected with the CMV virus.

Six weeks later, the animals' blood pressures were measured by the

cardiology team using a small catheter inserted in the mouse carotid artery. Among the mice fed a standard diet, the CMV-infected mice had increased blood pressure compared with the uninfected group. But even more dramatically, 30 percent of the CMV-infected mice that were fed a high-cholesterol diet not only exhibited increased blood pressure, but also showed signs of having developed atherosclerosis.

"This strongly suggests that the CMV infection and the high-cholesterol diet might be working together to cause atherosclerosis," says Crumpacker. In order to find out how and why this was occurring, the investigators went on to conduct a series of cell culture experiments.

Their first analysis demonstrated that CMV stimulated production of three different inflammatory cytokines - IL6, TNF□, and MCP1 - in the infected mice, an indication that the virus was causing inflammation to vascular cells and other tissues.

A second analysis found that infection of a mouse kidney cell line with murine CMV led to an increase in expression of the renin enzyme, which has been known to activate the renin-angiotensin system and lead to high blood pressure. Clinical isolates of human CMV in cultured blood vessel cells also produced increased renin expression.

"Viruses have the ability to turn on human genes and, in this case, the CMV virus is enhancing expression of renin, an enzyme directly involved in causing high blood pressure," says Crumpacker. When the scientists inactivated the virus through the use of ultraviolet light, renin expression did not increase, suggesting that actively replicating virus was causing the increase in renin.

In their final experiments, the researchers demonstrated that the protein angiotensin 11 was also increased in response to infection with CMV. "Increased expression of both renin and angiotensin 11 are important

factors in hypertension in humans," says Crumpacker. "What our study seems to indicate is that a persistent viral infection in the vessels' endothelial cells is leading to increased expression of inflammatory cytokines, renin and angiotensin 11, which are leading to increased blood pressure."

According to recent figures from the American Heart Association, one in three U.S. adults has high blood pressure, and because there are no known symptoms, nearly one-third of these individuals are unaware of their condition. Often dubbed "the silent killer," uncontrolled high blood pressure can lead to stroke, heart attack, heart failure or kidney failure, notes Crumpacker.

"We found that CMV infection alone led to an increase in high blood pressure, and when combined with a high-cholesterol diet, the infection actually induced atherosclerosis in a mouse aorta," says Crumpacker. "This suggests that further research needs to be directed at viral causes of vascular injury. Some cases of hypertension might be treated or prevented by antiviral therapy or a vaccine against CMV."

Source: Beth Israel Deaconess Medical Center