Researchers uncover new details behind inflammation that promotes heart disease

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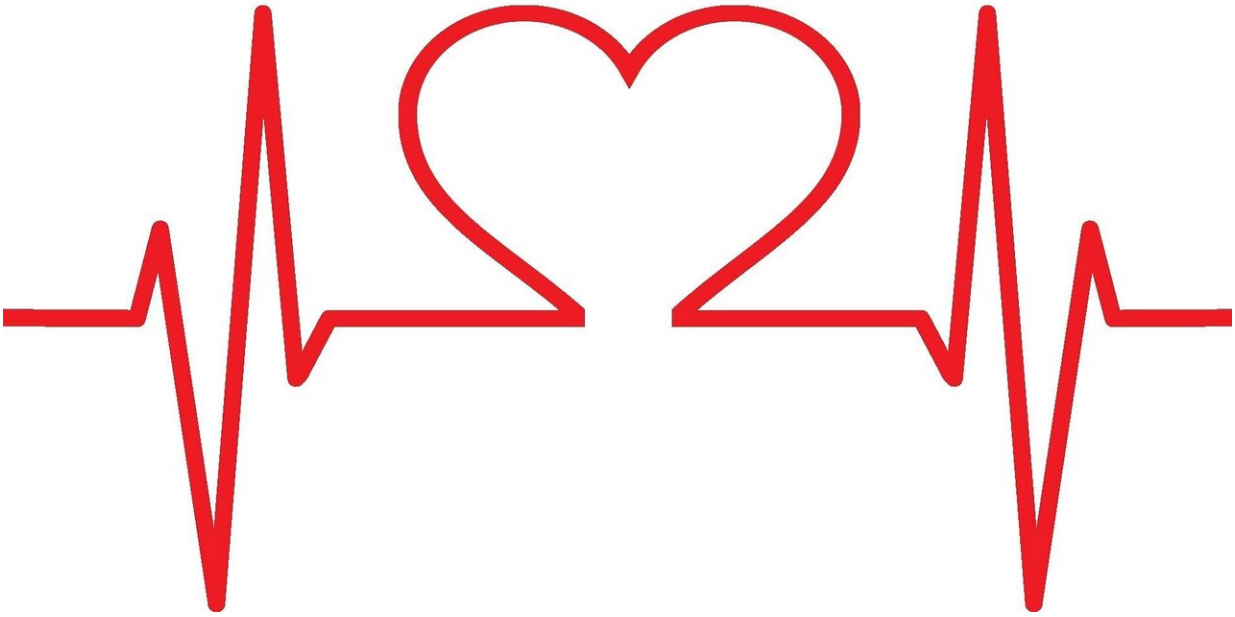

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High cholesterol and inflammation are key drivers of heart disease, and an inflamed buildup of lipids can cut off the blood supply through a coronary artery to cause a heart attack. Because white blood cells, which usually defend against infection, trigger inflammation in these situations, a team led by scientists at Massachusetts General Hospital (MGH) recently studied aspects related to the cells' production. The group's insights, which are published in *Nature Cardiovascular Research*, could

lead to new strategies to protect cardiovascular health.

"In patients with heart disease, white blood cells are more numerous," says senior author Matthias Nahrendorf, MD, Ph.D., an investigator in MGH's Center for Systems Biology and a professor of radiology at Harvard Medical School. "Many of these cells can be found in a plaque—the buildup of fats, cholesterol, and other substances in a blood vessel—where they arrive after being born in the bone marrow and migrating through the blood stream. But what leads to their increased bone marrow output is not clear."

Through experiments conducted in human bone marrow and mice, Nahrendorf and his colleagues found that high blood pressure, atherosclerosis, and the occurrence of a heart attack each can cause changes in the number of blood vessels in the bone marrow. These hallmarks of cardiovascular disease also changed the bone marrow vessels' structure and function and affected their release of factors that regulate white blood cell production and migration.

"As a consequence, more white blood cells were available in the body, and this increase, called leukocytosis, propels inflammation everywhere, including in the arteries and the heart," explains Nahrendorf. "This study will allow us to now examine how to reduce white blood cell production to normal values, thereby cooling off inflamed plaques anywhere in the body."

Co-authors include MGH's David Rohde, MD, Katrien Vandoorne, Ph.D. and others.

"This study provides strong evidence that cardiovascular disease affects the bone marrow vasculature and consequently blood stem cell activity," said Michelle Olive, Ph.D., program officer in the Division of Cardiovascular Sciences at the National Heart, Lung, and Blood

Institute, part of the National Institutes of Health. "This work sheds new light on the important role played by the vascular bone marrow niche and how inflammation occurs. It could lead to new targets and treatments for heart disease, the leading cause of death."

More information: Matthias Nahrendorf, Bone marrow endothelial dysfunction promotes myeloid cell expansion in cardiovascular disease, *Nature Cardiovascular Research* (2021). DOI: 10.1038/s44161-021-00002-8. www.nature.com/articles/s44161-021-00002-8

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