Bacteria eyed for possible role in atherosclerosis

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Dr. Emil Kozarov and a team of researchers at the Columbia University College of Dental Medicine have identified specific bacteria that may have a key role in vascular pathogenesis, specifically atherosclerosis, or what is commonly referred to as "hardening of the arteries" – the number one cause of death in the United States.

Fully understanding the role of infections in cardiovascular diseases has been challenging because researchers have previously been unable to isolate live bacteria from atherosclerotic tissue. Using tissue specimens from the Department of Surgery and the Herbert Irving Comprehensive Cancer Center at Columbia University, Dr. Kozarov and his team, however, were able to isolate plaques from a 78-year-old male who had previously suffered a heart attack. Their findings are explained in the latest *Journal of Atherosclerosis and Thrombosis*.

In the paper, researchers describe processing the tissue using cell cultures and genomic analysis to look for the presence of culturable bacteria. In addition, they looked at five pairs of diseased and healthy arterial tissue. The use of cell cultures aided in the isolation of the bacillus *Enterobacter hormaechei* from the patient's tissue. Implicated in bloodstream infections and other life-threatening conditions, the isolated bacteria were resistant to multiple antibiotics. Surprisingly, using quantitative methods, this microbe was further identified in very high numbers in diseased but not in healthy arterial tissues.

The data suggest that a chronic infection may underlie the process of

atherosclerosis, an infection that can be initiated by the systemic dissemination of bacteria though different "gates" in the vascular wall – as in the case of a septic patient, through intestinal infection. The data support Dr. Kozarov's previous studies, where his team identified periodontal bacteria in carotid artery, thus pointing to tissue-destructing periodontal infections as one possible gate to the circulation.

Bacteria can gain access to the circulation through different avenues, and then penetrate the vascular walls where they can create secondary infections that have been shown to lead to atherosclerotic plaque formation, the researchers continued. "In order to test the idea that bacteria are involved in vascular pathogenesis, we must be able not only to detect bacterial DNA, but first of all to isolate the bacterial strains from the vascular wall from the patient," Dr. Kozarov said.

One specific avenue of infection the researchers studied involved bacteria getting access to the circulatory system via internalization in white blood cells (phagocytes) designed to ingest harmful foreign particles. The model that Dr. Kozarov's team was able to demonstrate showed an intermediate step where *Enterobacter hormaechei* is internalized by the phagocytic cells, but a step wherein bacteria are able to avoid immediate death in phagocytes. Once in circulation, Dr. Kozarov said, bacteria using this "Trojan horse" approach can persist in the organism for extended periods of time while traveling to and colonizing distant sites. This can lead to multitude of problems for the patients and for the clinicians: failure of antibiotic treatment, vascular tissue colonization and initiation of an inflammatory process, or atherosclerosis, which ultimately can lead to heart attack or stroke.

"Our findings warrant further studies of bacterial infections as a contributing factor to cardiovascular disease, and of the concept that 'bacterial persistence' in phagocytic cells likely contributes to systemic dissemination," said Dr. Kozarov, an associate professor of oral biology

at the College of Dental Medicine. Dr. Jingyue Ju, co-author and director of the Columbia Center for Genome Technology & Bio-molecular Engineering, also contributed to this research, which was supported in part by a grant from the National Heart, Lung, and Blood Institute of the National Institutes of Health and by the Columbia University Section of Oral and Diagnostic Sciences.

More information: The article appeared in Volume 18 of the *Journal of Atherosclerosis and Thrombosis.*

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