

Biofilms, Lipoprotein Aggregates, Homocysteine, and Arterial Plaque Rupture

Uffe Ravnskov,^a Kilmer S. McCully^b

Independent Researcher, Lund, Sweden^a; Pathology & Laboratory Service, Veterans Affairs Medical Center, West Roxbury, Massachusetts, USA^b

The finding that bacteria form biofilms within the majority of carotid arterial plaques is a further demonstration of the important role played by microorganisms in the etiology of atherosclerotic vascular disease (1). Many investigators believe that the first step in atherogenesis is the creation of atherosclerotic plaques and that infection by microorganisms is a secondary phenomenon. In contrast, we believe that microbial infection is an essential component of the atherogenic process.

More than a dozen research groups have demonstrated that lipoproteins participate in the innate immune system by binding and inactivating microorganisms and their toxic products by forming circulating complexes (2–4). The size of these complexes may increase in cases of hyperhomocysteinemia, because homocysteine reacts with and causes aggregation of low-density lipoprotein (LDL). Autoantibodies may be created against homocysteinylated LDL, further enhancing the aggregation process. In addition, hyperhomocysteinemia causes endothelial dysfunction and narrowing of the lumens of capillaries and arterioles. In cases of chronic or severe acute infections, the complexes formed from microorganisms and aggregated LDL may obstruct arterial *vasa vasorum* because of high extravascular pressure and narrowing of vascular lumens. As *vasa vasorum* are end arteries, their obstruction by these aggregates may cause ischemic cell death of the arterial wall, leading to an intimal microabscess and creation of a vulnerable plaque (3). In support of this concept, several investigators have demonstrated that inflammation of the arterial wall first commences in the adventitia during atherogenesis. We believe that atherosclerosis is a scar phenomenon occurring during

the healing process after creation of the vulnerable plaque. Much clinical, epidemiological, and experimental evidence supports our hypothesis (3, 4). The findings of Lanter et al. (1) implicate dispersion of biofilms in the rupture of vulnerable plaques, producing such clinical manifestations of atherosclerosis as myocardial infarction, stroke, and ischemic gangrene.

REFERENCES

1. Lanter B, Sauer K, Davies DG. 2014. Bacteria present in carotid arterial plaques are found as biofilm deposits which may contribute to enhanced risk of plaque rupture. *mBio* 5(3):e01206-14. <http://dx.doi.org/10.1128/mBio.01206-14>.
2. Ravnskov U. 2003. High cholesterol may protect against infections and atherosclerosis. *Q. J. Med.* 96:927–934. <http://dx.doi.org/10.1093/qjmed/hcg150>.
3. Ravnskov U, McCully KS. 2009. Vulnerable plaque formation from obstruction of *vasa vasorum* by homocysteinylated and oxidized lipoprotein aggregates complexed with microbial remnants and LDL autoantibodies. *Ann. Clin. Lab. Sci.* 39:3–16.
4. Ravnskov U, McCully KS. 2012. Infections may be causal in the pathogenesis of atherosclerosis. *Am. J. Med. Sci.* 344:391–394. <http://dx.doi.org/10.1097/MAJ.0b013e31824ba6e0>.

Published 16 September 2014

Citation Ravnskov U, McCully KS. 2014. Biofilms, lipoprotein aggregates, homocysteine, and arterial plaque rupture. *mBio* 5(5):e01717-14. doi:10.1128/mBio.01717-14.

Copyright © 2014 Ravnskov and McCully. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Noncommercial-ShareAlike 3.0 Unported license](https://creativecommons.org/licenses/by-nc-sa/4.0/), which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original author and source are credited.

Address correspondence to Uffe Ravnskov, ravnskov@tele2.se.