

Atherosclerosis Pathogenesis and Microvascular Dysfunction

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To my patients and colleagues
Axel Haverich

To Orla and Kilian Graßl
Erin Colleen Boyle

Preface

Based on surgical observations, I've remained critical about many of the hypotheses regarding the pathogenesis of atherosclerosis, since two important paradigms appear to be incorrect. First, atherosclerosis is not a generalized disease as defined segments of the arterial tree in humans are nearly always disease-free. Second, disease is not instigated in the endothelium of the parent vessel. Growing evidence and my observations support an “outside-in” initiation and progression of atherosclerosis development whereby vascular inflammation is initiated in the adventitia and is propagated inward toward the intima. Cardiovascular surgeons from around the world would support this.

These observations led me on a 6-year journey of research via the Internet. Very soon, though, other sources like international libraries and historic bookshops were involved providing me with remote articles and “ancient” books from the nineteenth and early twentieth centuries. I drew upon these to form the picture of the pathogenesis of atherosclerosis presented in this book. Relating my theory of atherosclerosis development over coffee one morning in Bad Nauheim, my mentor, the former director of the Max Planck Institute for Heart and Lung Research, Wolfgang Schaper, smiling broadly said, “I've worked my whole life on this topic and you've explained the whole thing in 10 minutes!” Encouraged, I next did what you always should do—I listened to an old friend, Davor Solter, a Croatian stem cell researcher and also a former Max Planck Director. When I approached him with my ideas, he immediately suggested that I compile all my findings in a book. I desperately resisted, referring to the tremendous clinical burden, being head of a busy cardiothoracic, vascular, and transplant unit. However, it would have been impossible to provide sufficient insight into the topic for the reader by an original article, a review article, or a historic note. Most surgical friends remained skeptical, only Gerd Walterbusch, my Doktorvater, surgical mentor, and long-time close friend remained a critical advisor, emphasizing the role of the lymphatic system in atherosclerosis.

The ideas put forth in this book are important for our research on primary and secondary prevention of atherosclerosis, for our trajectories in clinical diagnostics and therapy development, and finally for the patients and their families affected

by this highly prevalent and deadly disease. Therefore, with the help and enthusiasm of Erin Boyle, I finally gave in and we've worked together on translating these ideas into a book. I am indeed very grateful to her because without her help in writing and completing the literature research, the book would not have been finalized until my retirement. Explanation of the molecular mechanisms involved in vasa vasorum dysfunction and protection, especially in Chap. 6, goes back primarily to Erin's research. And finally, Erin and I would like to thank Birgit Lüttig for her editorial assistance in completing this project and Daniela Martens for help with the illustrations.

Hannover, Germany
February 2019

Axel Haverich

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