Book review


This multiauthored book consists of ten chapters which together provide a comprehensive review of various evidence that is mainly in support of the hypothesis of a role for some viral infections in the initiation and progression of atherosclerosis, restenosis and allograft vasculopathy. The authors are among the foremost workers in this field. One chapter comes from the Netherlands. The others are from the United States.

The volume is dedicated to Earl Benditt and eight of the chapters allude to his hypothesis of the monoclonality of atherosclerotic lesions including the first chapter (Schwartz and Murry) which revolves around the hypothesis and the diversity of arterial smooth muscle cells. The monoclonal hypothesis of atherogenesis postulates that single smooth muscle cells (or at most a few) in the arterial wall may acquire proliferative advantage over those in the surrounding tissue following alterations in the cell’s genome. Alterations in the cell’s genome might be the consequence of viral invasion following earlier colonization of overlying endothelial cells. According to the hypothesis, the focal smooth muscle cell-rich thickenings of the intima that are ubiquitous in many arterial segments from birth may have been generated in this way and may represent the first step (or a prerequisite) in the development of obstructive atherosclerotic lesions.

The view that these focal intimal thickenings are the initial lesions of atherosclerosis is shared by the response to injury hypothesis. In the view of this latter hypothesis a range of external injurious agents may produce endothelial cell dysfunction which, this particular hypothesis assumes, translates into arterial smooth muscle cell migration and proliferation. In fact, evidence that factors other than external injurious agents produce the focal intimal thickenings is better established. This evidence indicates that the thickenings are necessary localized adjustments (adaptations) of the lumen by the vessel to disparities in fluid mechanical forces around a vessel circumference in segments with orifices and bifurcations (Atherosclerosis 1987; 64:91, Circulation 1992; 85:391). A subgroup of such adaptive intimal thickenings does indeed coincide with sites at which more lipid and macrophage foam cells accumulate and at which atheroma develops first when atherogenic lipoproteins and blood pressure are adequately high. However, when atherogenic lipoproteins are very high (as in familial hypercholesterolemia homozygotes), atheroma develop quickly also in arterial segments without adaptive intimal thickenings, indicating that the latter are not a prerequisite for atheroma formation. Furthermore, the histology of adaptive intimal thickening is orderly and appropriate to arterial structure and in no way resembles that of lyomyomas or other tumors. Referring to adaptive thickenings as ‘intimal cell masses’ ignores the functional histological arrangement of their cells and intercellular matrix. Their thickness in proportion to the media is already established at birth and there is no evidence that they grow disproportionately rapidly in the first months of life.

In chapter 2, Shih promotes Japanese quail as an ideal species for the study of the possibility of a role of viral infection in atherogenesis. The author speculates that atherosclerosis-susceptible quail might be latently infected with a putative quail herpes virus. Marek disease virus-induced lesions of chickens are also described in chapter 2 while pictures of such lesions are included in chapter 10.

In chapter 3, Melnick and co-authors review studies of human cytomegalovirus (HCMV) and atherogenesis and particularly their work in patients undergoing vascular surgery. The arterial tissues of these patients were positive for CMV nucleic acid more often than matched controls. Furthermore, atherosclerotic patients were seropositive for HCMV more often than controls.

In chapter 4, Bruggeman writes on the susceptibility of endothelial cells to CMV infection in the immunosuppressed host, the susceptibility of smooth muscle cells when endothelium is lacking and on the role of CMV infection in allograft vasculopathy (sometimes called ‘transplant-associated atherosclerosis’).

In chapter 5, Epstein et al. explore the possibility that HCMV infection contributes to the smooth muscle cell proliferation that constitutes the restenosis that may follow percutaneous interventions. Putative molecular mechanisms and epidemiologic data that support an association are discussed.
In chapter 6, Bonin and McDougall add a cautionary note to the viral hypothesis of atherogenesis. Questions are raised about HCMV as a mutagen for smooth muscle cells.

Chapter 7 (Nachtigal) reviews in vitro studies of the induction of heritable phenotypic changes (escape from senescence or 'immortalization') in rabbit aortic smooth muscle cells with a simian virus and certain human herpesvirus regions.

In chapter 8, Kefalides and Ziaie review in vitro studies of the effect of herpes simplex virus infection on endothelial and smooth muscle cell synthesis of matrix proteins including the synthesis of altered extracellular matrix components.

The authors of chapter 9 (Moldow and Vercelotti) review in vitro studies that indicate that virus-infected endothelium is more adhesive for white blood cells, has procoagulant consequences by generating thrombin and allows adhesion of activated platelets.

In chapter 10, Nicholson and Hajjar discuss mainly the effect of in vitro herpesviral infection on the cholesterol metabolism of vascular smooth muscle cells and on the anticoagulant functions of vascular endothelium.

The chapters contain some duplication as the same underlying premises are reviewed by most authors as a background to and justification of their own work. The book is nevertheless an excellent guide to data that mainly support the role of some viral infections in atherogenesis and in related vascular problems.

Herbert C. Stary
Department of Pathology
School of Medicine
Louisiana State University
1901 Perdido St.
New Orleans, LA 70112
USA