

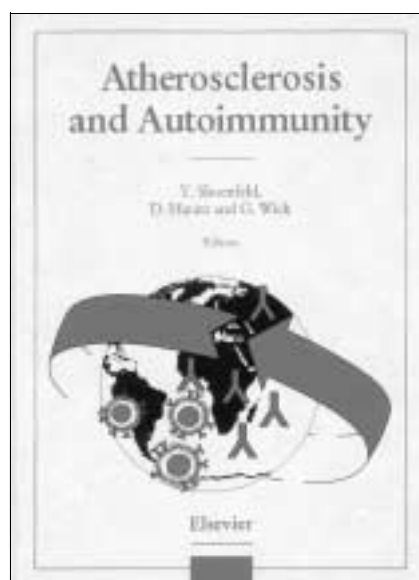


Atherosclerosis And Autoimmunity

Edited by Yehuda Shoenfeld, Dror Harats and Georg Wick

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Atherosclerosis (AS) is a disease process that afflicts millions of people worldwide and is the number one killer in the western hemisphere. The World Health Organization projects that AS will become the leading cause of death in the third world by the year 2020. Much research was invested in the twentieth century in an effort to understand the pathophysiology of this devastating disease.

Many risk factors for AS have been identified and recent evidence has convincingly implicated inflammatory reaction as the major underlying cause for the AS disease process. The main culprits implicated as the inciting agents of AS have been the traditional risk factors for AS, such as low density lipoprotein-cholesterol (LDL-C), cigarette smoking, hypertension, diabetes mellitus and acute stress.

More recently, new exciting data have linked additional risk factors to AS, such as homocysteinemia and infectious agents, both viral and microbial. The mechanisms by which these risk factors have initiated or accelerated the disease process have been best described by the “response to injury” hypothesis formulated by Ross. According to this theory, these different factors exert toxic effects on the endothelial cells (EC) lining the arterial luminal wall, causing denudation or dysfunction of the EC. The dysfunctional EC are rendered incapable of efficiently performing their main task, i.e., serving as a permeable barrier enabling LDL-C molecules and monocytes to penetrate the arterial subendothelial intima. This triggers a host of inflammatory reactions that are responsible for the formation of the earliest AS lesion, the fatty streak described by Ross as a pure inflammatory/immunological lesion. Thereafter, immunological processes – both cellular and humoral – different cytokines, platelets and coagulation system factors, growth factors, physical stresses and additional factors interact over many years to further promote the AS disease to its culmination in the complex and/or unstable plaque. This hypothesis is firmly based on a plethora of experimental, clinical and epidemiological data gathered throughout the twentieth century. Interestingly, the implication of autoimmunity as a possible protagonist in the AS process was suggested only about a decade ago by Dr. G.

Wick, one of the editors of this important book.

In *Atherosclerosis and Autoimmunity*, the editors have undertaken the formidable task of collating all current knowledge and hypotheses regarding this new and exciting field. All three editors, two of whom are Israeli, have contributed substantially to the unraveling of the AS and autoimmunity connection. Being instrumental in the field, they were able to gather articles by leading international investigators, under one ‘roof’, and compose a comprehensive textbook encompassing state-of-the-art basic, clinical, genetic and epidemiological data.

The book consists of seven parts: the first is dedicated to the description of basic concepts of autoimmunity and AS. Dr. Wick brilliantly describes one of his major innovations in the field, namely, the role of autoimmune reaction towards arterial wall heat shock protein (HSP) 60 in the initiation of the AS lesion. The second describes the pathogenetic immune mechanisms of AS, which includes an in-depth description of the connection between lipids, AS and immunity, and the role of apoptosis and certain antimicrobial peptides (the defensins) in AS and autoimmunity. The third deals with the newly described relationship between infection and AS and how it is mediated by immune mechanisms. The fourth describes a host of different autoantibodies implicated in the AS process. Among the antigens responsible for the formation of the autoantibodies are oxidized LDL, endothelial

cells, phosphocholine and prothrombin. The Shoefeld and Harats cooperation in exposing the autoimmune mechanisms underlying the HSP and B2GP1 antiphospholipid antibody in the pathogenesis of AS is clearly delineated. The fifth, edited by different editors, is dedicated to a detailed description of the role of anti-EC antibodies in AS. I was particularly impressed by the *in vitro* salutary effects of IVIg on the EC, which certainly deserve clinical investigation. The sixth describes how traditional

autoimmune diseases, such as systemic lupus erythematosus, antiphospholipid syndrome, rheumatoid arthritis, vasculitis and familial Mediterranean fever may be involved in triggering AS disease. This part is particularly interesting for clinicians involved in the treatment of the consequences of AS and those caring for patients suffering from autoimmune diseases. The last part describes the genetics of arterial thrombosis.

As can be seen from this brief description, this comprehensive book is

an invaluable source for the understanding of the principles, basic mechanisms and potential clinical implications of autoimmunity and AS. It is recommended for those who might be interested in this new field, such as internists, immunologists, hematologists, lipidologists and cardiologists.

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