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# Recent views on cytohistological characteristics and pathogenic mechanisms of atherosclerotic lesions types I, II and III

## Savremeno shvatanje citoloških karakteristika i patogenih mehanizama aterosklerotskih bolesti tipa I, II i III

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### Introduction

Contemporary model of the pathogenesis of atherosclerosis is based on the hypothesis that local damage of the endothelium together with systemic factors such as hypercholesterolemia, hyperglycemia, hypertension, chronically infections, genetic factors, *diabetes mellitus*, initiate a cascade of processes which eventually cause atherosclerotic lesion development [1, 2].

Although various hypotheses are already known about the pathogenesis of atherosclerosis and different factors of predisposition have been studied, from the point of molecular and vascular biology to clinical presentations and therapy methods, in modern literature there are still opposing views about the initial moment in the pathogenesis of this condition, regarding its functional and morphological changes.

### The stage of the initial lesion - early lesion (type I)

*Activation of endothelium*

The initial stage, which precedes the development of atherosclerosis, is endothelial dysfunction, namely, activation of endothelial cells as a specific response to the action of harmful agents. Acute response of endothelium results in inflammation, coagulation disorders and vasomotor changes. The release of inflammation mediators deposited in the Weibel Palade bodies represents a very quick response of endothelial cells [3]. One of the most important consequences of endothelial activation is a decreased NO production, which causes the absence of its antiatherogenic, antiproliferative and vasodilatatory effects and, also, causes an increased production of endothelin-1 (ET-1) which in turn, through its mitogenic effect, stimulates proliferation of smooth muscle cells (SMCs) in the intima, and consequently initiate atherosclerosis [4, 5].

During activation of endothelial cells, changes in the process of coagulation have also been observed. Endothelial cells modulate their phenotype from anticoagulative to procoagulative, through an increased expression of tissue factors, or increased release of tissue plasminogen [6, 7].

Besides alterations in tonus and coagulation, endothelial activation includes increased expression of adhesive proteins (P-selectin, integrins) which promote the adhesion of leukocytes on endothelium and their infiltration in the subendothelial connective tissue [8]. This results in the release of free radicals, proteases and elastases which lead to further damage of endothelial cells [7].

*Accumulation of lipids in the intima*

The first step in the development of atherosclerosis is the accumulation of lipid droplets in the intima of the vessel

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