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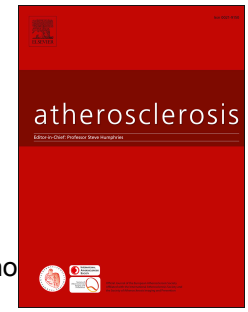

Quit smoking to outsmart atherogenesis: Molecular mechanisms underlying clinical evidence

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Atherosclerosis is a multifactorial pathological process, during which the physiological composition of arterial walls is structurally and functionally altered. The atheroma growth - accumulation of fibro-adipose and degenerative material in the artery walls – leads to the stiffening of vessels and the narrowing of the lumen, limiting the blood flow. Such reduction of blood flow represents only the initial complication of the formation of the atherosclerotic plaque whereas the persistence of the insult, with the hemodynamic instability that characterizes the atherosclerotic artery, can induce evolution of the plaque *versus* an instable phenotype with major vulnerability and probability of rupture[1]. The atherosclerotic plaque rupture leads to the exposure of the highly thrombogenic necrotic core material, with subsequent platelet activation and formation of thrombi that can block blood flow *in loco*, or break away and enter in the bloodstream, obstructing other vessels with smaller diameter. Therefore, the atherosclerotic process can cause coronary artery disease (CAD), ischemic stroke, and peripheral artery disease, representing a major life-threatening disorder.

The main risk factors underlying the development of the atherosclerotic plaque are:

1) Elevated blood levels of lipids; essentially cholesterol in LDL form, which can deposit along arterial wall and, in combination with oxidative stress, can cause endothelial leak, with incorporation of the lipids inside the intima of the vessel.

2) High blood pressure; the exposition of endothelium to constant high pressure can trigger atheroma neo-formation; moreover, the hemodynamic instability derived from suddenly high pick of blood pressure, can also represent an insult for pre-existent plaque, causing its rupture.

3) Tobacco smoking; both above risk factors are exacerbated by smoke through its ability to potentiate hypertension, and to affect lipid metabolism increasing LDL levels. Cigarette smoke represents an independent risk factor for atherosclerosis, since chemical constituents of smoke have high oxidant and inflammatory power that can directly induce endothelial damage and potentiate inflammatory response.

Smoking and atherosclerosis: direct proportionality?

Smoke has a profound effect on vessel homeostasis through the activity of single smoking compounds