The Influence of Endothelial Dysfunction in Atherosclerosis: Mathematical Modeling

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Abstract: Atherosclerosis has traditionally been viewed just as deposition of lipids within the vessel wall of medium-sized and large arteries. Recently, biological observations show that endothelial dysfunction play a fundamental role in the initiation and progression of atherosclerosis as an inflammatory disease. High low-density-lipoprotein (LDL) concentration alter the endothelial layer permeability (by creating leaky junctions between endothelial cells), contributing to the subsequent accumulation of lipids in the inner layer of the blood vessel (tunica intima), where, consequently, the atherosclerotic plaque will form and grow.

In this talk we will present a mathematical model for the early stage of atherosclerosis, as a chronic inflammatory disease, in particular on the following sub-processes: dynamics of LDL and oxidized LDL, influencing the endothelial permeability; transport of monocytes from blood flow into the intima; formation of foam cells due to macrophages ingestion of oxidized LDL. The model consists of partial differential equations: Navier-Stokes equations modeling blood flow, Biot equations modeling the fluid flow inside the poroelastic vessel wall, and convection/chemotaxis-reaction-diffusion equations modeling transport, signaling and interaction processes initiating inflammation and atherosclerosis. The main innovations of this model are: a) quantifying the endothelial permeability to LDL and to monocytes as a function of WSS, cytokines and LDL on the endothelial surface; b) transport of monocytes on the endothelial surface, mimicking the monocytes adhesion and rolling; c) the monocytes influx in the lumen, as a function of factor increasing monocytopoiesis; d) coupling between Navier-Stokes system, Biot system and convection/chemotaxis-reaction- diffusion equations. Numerical simulations of a simplified model performed in an idealized two dimensional geometry aiming to demonstrate some important features of the early atherosclerosis process, also will be presented.

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