Abstracts

The vascular endothelium: basic and clinical aspects

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The vascular endothelium: Structural, functional and pathophysiological aspects

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The endothelium is an organ with a large surface (~350 m²) and a comparatively small total mass (~110 g) which plays a central role for regulation of perfusion, fluid and solute exchange, haemostasis and coagulation, inflammatory responses, vasculogenesis and angiogenesis. Between vessels and organs, the endothelium differs in its morphology ("continuous", "fenestrated" or "discontinuous") and functional properties (e.g. permeability, expression of surface molecules, responses to hemodynamic forces, pacemaker cells). For example, there are marked structural and functional differences between the endothelial lining of the lung and the brain. In the pulmonary endothelium, the level of adhesion molecule expression is constitutively high, allowing to maintain a large pool of marginated leukocytes. Endothelial cells in the brain are characterized by the lack of fenestrations and an elaborate system of tight junctions limiting and controlling exchange with the interstitial compartment.

A central component of endothelial function in many organs is the release of active substances in response to chemical agonists and to hemodynamic forces, including NO, prostacyclin and EDHF (endothelium derived hyperpolarizing factor). These substances control vascular tone, but also structural vascular adaptation, proliferation, and inflammation. In recent years, it became increasingly clear that the luminal endothelial surface is covered with a gel-like layer exhibiting a thickness in the range of 0.5 to 1 µm. This layer has been named endothelial surface layer (ESL) and is much thicker as compared to the so called glycocalyx which consists of proteoglycans and glycoproteins anchored in the endothelial plasma membrane (typical thickness of about 50-100 µm). While the composition of the ESL still remains largely elusive, adsorbed plasma proteins and hyaluronan seem to be essential. Due to its wide ranging roles for fluid exchange, flow resistance, oxygen transport, vascular control, coagulation, inflammation, and atherosclerosis, the ESL will be a relevant focus for future studies in endothelial function.

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Effects of shear stress on endothelial activation and vascular inflammation

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Atherosclerosis is a chronic lipid-driven inflammatory disease of arteries that causes heart attack or stroke. Early lesions (fatty streaks) contain monocytes and T lymphocytes which are recruited from the circulation to activated vascular endothelial cells (EC) which express adhesion molecules (e.g. E-selectin, VCAM-1) and chemokines (e.g. IL-8, MCP-1) at their surface. This process relies on dual activation of NF-κB and MAP kinase – AP-1 signaling pathways which leads to transcriptional activation of pro-inflammatory genes. Hemodynamics play a central role in regulating vascular inflammation and atherosclerosis which occurs predominantly at branches and bends of the arterial tree that are exposed to relatively low or re-circulating blood flow. In contrast, regions of the arterial tree with uniform geometry that are exposed to high rates of unidirectional flow are protected from inflammation and atherosclerosis. Blood flow exerts shear stress (mechanical drag) at the interface between blood and the endothelial layer, where it induces a shearing deformation of the endothelial cells. Thus protected regions of the arterial tree with uniform geometry are exposed to high