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An in vitro model to study the passage of macromolecules through human arterial endothelial cell monolayers. Effect of vasoactive substances.

The endothelium controls the influx of macromolecules into the arterial wall and other tissues, a process that is disturbed in various pathological conditions. We have developed an in vitro model to study the passage of macromolecules through human arterial endothelial cell (EC) monolayers in vitro and studied the effect of vasoactive substances on the barrier function of the EC.

Human umbilical artery EC cultured on fibronectin-coated polycarbonate filters form a tight monolayer and have a transendothelial electrical resistance (TEER) of 17 ± 4 Ohm.cm^2. The presence of serum proteins and Ca^{++}-ions was needed to keep the monolayers intact for prolonged time. The passage of ^{125}I-LDL proceeded linearly in time and was 60-180 fold slower through EC than through unseeded filters. No saturation of the passage process was observed between two and four hours after addition of various concentrations LDL (25-800 µg protein/ml) and a fixed amount of peroxidase (5 µg/ml). However, during the first hour after addition a reduced passage rate of both LDL and peroxidase was observed in presence of high concentrations LDL, resulting in an apparent saturation of the passage process. Methylated LDL and Lp(a) passed at the same rate as equivalent amounts of LDL; acetylated LDL two-fold slower. The monolayers displayed molecular sieving characteristics towards proteins and dextrans of various molecular weights (9 kD - 2000 kD).

Addition of histamine to human umbilical, carotid artery and aortic EC resulted in a 2-5 fold increase in the passage rate of LDL and a 32% reduction of the TEER. This process was reversible and mediated via H1-receptors. Small gaps between EC became visible on E.M.-examination. Thrombin and Ca^{++}-ionophore increased the passage through EC layers for prolonged time. The effects of histamine and thrombin were paralleled by a rapid and marked increase in cytoplasmatic Ca^{++} level of the EC (fura-2 assay). These observations fit in a model, in which these agonists cause an increase in cytoplasmatic Ca^{++} level, which results in a contraction of EC and an increase of the permeability of the monolayers.

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