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ROLE OF ENDOTHELIAL INTEGRITY IN ATHEROSCLEROSIS. Stephen M. Schwartz, Corinne M. Gajdusek, M.A. Reidy; Department of Pathology; School of Medicine; University of Washington; Seattle, WA 98195 USA

The current view of the pathogenesis of atherosclerotic lesions stresses loss of endothelial integrity as a major event leading to the three major events in lesion formation...accumulation of smooth muscle cells, accumulation of lipid and accumulation of platelets. Recent advances in endothelial biology, however, suggest that frank denudation may not exist. Our kinetic studies of small wounds to endothelium both *in vivo* and *in vitro* demonstrate the ability of the endothelium to rapidly replace desquamating cells. Furthermore, these small areas of mechanical denudation do not stimulate smooth muscle proliferation. Finally, careful studies of hyperlipemic and hypertensive animals have failed to demonstrate any actual denudation.

The possibility remains that denudation occurs repeatedly, with extremely brief periods of subendothelial exposure. Thus lesion formation could represent the cumulative record of multiple, tiny incidents. This hypothesis is, however, difficult to test. Less dramatic forms of injury which may be of interest include alterations of endothelial cell functions in replicating cells as well as alterations in function which may occur independent of any cell loss. This last category receives new emphasis today because of the rapid increase in the number of functions identified in endothelial cells. These include the apparent ability of endothelial cells to synthesize a growth factor which can stimulate smooth muscle proliferation in the absence of the platelet derived growth factor.

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MECHANISMS OF VIRAL-INDUCED ENDOTHELIAL INJURY. H.M. Friedman. Department of Medicine, University of Pennsylvania, Philadelphia, PA.

We examined the role of common human viruses as inducors of injury to human umbilical vein or bovine-thoracic aorta endothelial cells grown *in vitro*. Indicators of infection included endothelial cytopathology, viral replication and viral antigen detection by immunofluorescence. Herpes simplex, adeno, measles and parainfluenza viruses infected both human venous and bovine aorta cells. Mumps, polio, and echo 9 viruses grew only in human venous cells, while coxsackie B4 replicated only in bovine aorta endothelium. Several viruses (CMV, influenza A, RSV) infected neither type of endothelial cell.

We examined one virus, herpes simplex type 1 (HSV) in some detail and showed that HSV can establish a persistent infection of bovine aorta endothelial cells *in vitro*. When HSV was inoculated at a multiplicity of infection (MOI) of 0.1, the amount of infections virus produced by the culture fluctuated over a 3 month period. By the third week after inoculation the endothelial monolayer had recovered and no infectious virus was detected for an additional 2 months. However, by the third month, typical herpetic changes reappeared, 10^3 plaque forming units of intracellular and supernatant virus was detected, and by infectious cell center assays, approximately 1% of cells produced virus.

In separate experiments, human umbilical vein endothelial cells were inoculated with HSV (MOI of 1.0) and examined for induction of surface receptors for the Fc portion of IgG and for C3b. Using ^{51}Cr-labeled sheep erythrocytes coated with IgG or with IgM and purified complement components (C_1, C_4, C_2, C_3) an Fc and C3b receptor were detected on the infected cells. These receptors were distinct from one another as demonstrated by blocking experiments using purified Fc fragments, and consisted, at least in part, of viral antigens since antibody to HSV blocked function of both receptors.

These studies demonstrate that viruses can produce acute or persistent infection of endothelial cells and can induce receptors for IgG and complement on the cell's surface.