

INVITED SYMPOSIUM X

The Role of Endothelial Cells in Hemostasis.

EXPERIMENTAL THROMBOCYTOPENIA: AMELIORATION OF ENDOTHELIAL PATHOLOGY AND BLEEDING BY PREDNISONE. Craig S. Kitchens and Leon Weiss. Veterans Administration Hospital and University of Florida, Gainesville, Florida, and University of Pennsylvania, Philadelphia, Pennsylvania, U.S.A.

Experimental thrombocytopenia results in endothelial alterations associated with bleeding. In this study, we show that prednisone (Pred) may prevent and reverse these changes supporting inference that Pred decreases capillary fragility. Rabbits (3-4 kg) given busulfan developed a 98-99% reduction in platelet count and hemorrhaged profusely. Oral Pred (0.2mg/kg or 1.0mg/kg/day) reduced hemorrhaging despite persistent thrombocytopenia. Tongue biopsies on the third Pred day were examined by EM. Normal animals served as control, one normal group received 1.0mg/kg Pred daily, one thrombocytopenic group received no Pred, and one group received Pred while thrombocytopenia was induced. 100 consecutive capillaries or venules of each preparation were examined for fenestrations, "thin spots", (≤ 800 Å thick), and mean thickness as determined by planimetry.

Preparation	Animals	Vessels	Thickness	SEM, Å	"Thin Spots"	Fenestrations
Control	4	100	4254 ± 105		0	0
Control + Pred	4	100	3978 ± 59		0	0
Thrombocytopenia	4	100	2081 ± 218		33	9
Pred then Thrombocytopenia	4	100	3635 ± 77		5	0
Thrombocytopenia, LO Pred	4	100	3556 ± 40		8	1
Thrombocytopenia, HI Pred	4	100	3704 ± 206		3	3

All preparations demonstrated normal endothelial junctions. We hypothesize that the bleeding of thrombocytopenia is caused by altered capillary and venule endothelium and that diminished bleeding observed with Pred administration is caused by alteration of these endothelial changes.

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A major hypothesis of atherogenesis ascribes endothelial damage as a causation of intimal proliferation which may, in turn, be a progenitor of arteriosclerosis. This hypothesis appears substantiated by experimental evidence varying from immunologic to mechanical damage of endothelium as a means of inducing both diffuse and focal intimal proliferation. There appears, in addition, other influences exerted by endothelial cells on the pathophysiology of intimal thickening. During intimal healing after wide spread endothelial denudation by an intra-arterial balloon catheter, endothelial regrowth seems to promote regression of intimal thickening. It is not clear if this diminution of thickness is due to reduction in cells, extracellular material, or both.

However, diminution of intimal thickening is not a feature of the healing process in the presence of hyperlipidemia. With widespread de-endothelialization, as described above, areas beneath regenerating endothelium are much thicker, and show a marked predisposition for the accumulation of lipid into the underlying already thickened intima. What physiologic or metabolic influences are exerted by the endothelium under these circumstances are unclear, but, the presence of endothelium may be a highly significant factor in the natural history of intimal proliferation and atherogenesis.