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INVITED SYMPOSIUM II

Platelet-Lipid Interactions in Atherosclerosis.

PLATELET FUNCTION IN HYPERBETALIPOPROTEINEMIA. Robert W. Colman, Dept. of Med. and Path., University of Pennsylvania, Philadelphia, Pennsylvania.

Individuals with familial hyperbetalipoproteinemia are at increased risk of premature atherosclerosis and thrombosis. Although there is controversy whether platelet survival is shortened or normal in this disease, several *in vitro* tests of platelet function after stimulation with ADP including electrophoretic migration, platelet factor 3, aggregation response and release of nucleotides have been found to be increased. These functional changes are accompanied by an increase of cholesterol to phospholipid ratio in the platelet membrane. Clofibrate and halofenate reverse some of these abnormalities *in vitro* and the former drug, when administered for 6 weeks to patients with type IIa hyperlipoproteinemia decreases platelet sensitivity to ADP and epinephrine. The platelet hypersensitivity to aggregating agents can be reproduced *in vitro* by increasing the cholesterol to phospholipid rather in normal platelets. These artificially hypersensitive platelets can be returned to normal by halofenate *in vitro*. Incorporation of cholesterol into platelet membranes increases the basal level of the membrane associated enzyme adenylate cyclase. However, the enzyme no longer responds to stimulation by prostaglandin E_1, and this is associated with relative resistance of the platelet to inhibition by this pharmacologic agent. These functional alterations produced by cholesterol enrichment of platelet membranes occur in parallel with an increase in platelet membrane microviscosity suggesting that the more rigid membrane can alter the behavior of membrane associated enzymes and receptors.

THE VON WILLEBRAND PIG AS A MODEL FOR ATHEROSCLEROSIS RESEARCH. V. Fuster, E.J.W. Bowie and J.C. Lewis. Mayo Clinic and Mayo Foundation, Rochester, Minnesota, U.S.A.

The aortas of 11 pigs with homozygous von Willebrand's disease (vWd) were compared with those of 11 normal pigs, all aged 1 to 3 years. Six of the controls exhibited multiple arteriosclerotic plaques over 2 mm. in diameter with intimal thickenings of 63 to 130 microns. In contrast, none of the vWd pigs had multiple plaques; one had a single lesion over 2 mm. in diameter.

Ten additional pigs, 5 controls and 5 with homozygous vWd, were placed on a 2% cholesterol diet for 6 months, beginning at the age of 3 months. Four of the controls developed aortic arteriosclerotic lesions exceeding 7.5% of the entire surface. Intimal thickness ranged up to 370 microns. In contrast, 4 of the vWd pigs developed lesions not exceeding 0.5% of the aortic surface; the fifth vWd pig had arteriosclerotic lesions involving 7.3% of the aortic surface.

The aortas of the vWd pigs did stain with Evans blue dye injected antemortem, and they exhibited fatty infiltration in the intima. By electron microscopy, severe endothelial damage was apparent, but there was no intimal proliferation.

The vWd pig seems to be an ideal model for arteriosclerosis research and the possible relationship of our findings may be related to impaired platelet-arterial wall interaction in vWd.