ENDOTHELOTROPIC DRUGS - STABILIZERS OF THE ENDOTHELIAL LINING AGAINST DESQUAMATION.

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On the basis of a new test for counting circulating endothelial cells in blood, a group of drugs was redefined which prevent endothelial desquamation after a standard intravenous injection of citrate into rats. The group comprised practically all drugs designated as venotonics or vitamin P-active agents, including some haemostatics, analgesic-antipyretics (acetylsalicylic acid) and some antiatherosclerotics (pyridinolcarbamate, clofibrate). A marked activity was observed also with several calcium-antagonists (nifedipine, prenylamine, chromonar, dipyridamole and verapamil). Many endothelotropic drugs are simultaneously effective in blocking platelet functions. The suggested common mechanism of action is the influence on the consistency of the cellular surface coat (endothelia cement).

PLATELET AGGREGATION IN HEART DISEASE. K. Oversohl, W. Theiss, C.S. So and K.F. Seidl.

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Increased platelet adhesion and aggregation has been reported in patients suffering from rheumatic valvular heart disease and from atherosclerotic heart disease. We therefore measured spontaneous aggregation "PAT III" (Breddin) and ADP-induced platelet aggregation (Born) in 141 patients who underwent cardiac catheterization. There were 50 patients with coronary heart disease, 41 with valvular heart disease, 18 with cardiomyopathy; 32 with normal findings at catheterization served as control group.

In comparison to controls, patients with coronary heart disease had significantly increased aggregation. Subdivision into 1, 2, or 3 vessel disease revealed no significant differences. Patients with valvular heart disease also had significantly increased aggregation. This appears to be particularly the case after valvular grafting. Cardiomyopathies were not associated with increased platelet aggregation.

ALTERATION OF PLATELET CYCLIC AMP (cAMP) BY ETHANOL. D.H. Cowan, M. Kikta, and D. Baunach. Case Western Reserve University, Cleveland, Ohio, U.S.A.

Studies of cAMP in human platelets exposed to ethanol were done to assess one possible mechanism for ethanol-related platelet dysfunction. Ingestion of ethanol by 3 subjects produced blood ethanol levels from 65-76 mM. Thrombocytopenia occurred in 1 subject and impaired platelet function occurred in all. Platelet cAMP decreased 36, 51, and 59% below control levels. Infusion of ethanol to 2 normals produced blood ethanol levels of 43 mM and decreased platelet cAMP by 15% and 22%. Incubation of normal platelets with 86 mM ethanol in vitro decreased cAMP from 13.8 ± 2.9 (1 SD) to 9.4 ± 3.5 ($p < 0.02$). By contrast, ethanol did not impair the increase in cAMP that occurred with $1.3 \mu\text{M}$ PGE₁. Further, ethanol enhanced the increase in cAMP produced by 2.0 mM papaverine (Pap) by 160-220% and that produced by Pap + PGE₁ by 58%. Dopamine, 0.1 mM, caused a 23% decrease in the basal level of cAMP, a 31% decrease below the subnormal level of cAMP seen with ethanol alone, and a 41% reduction in the increased level of cAMP produced by Pap + ethanol. The effect of ethanol on platelet cAMP metabolism is complex. Ethanol reduces basal levels of cAMP, does not decrease elevated levels that result from PGE₁ stimulation of adenylate cyclase, and augments the inhibitory effect of Pap on platelet phosphodiesterase (PDE). Despite causing a decrease in basal cAMP levels, ethanol may impair platelet function by potentiating the effect of agents or other conditions which increase cAMP. The effect of ethanol on Pap-stimulated PDE activity may be blocked by dopamine, a neuropharmacologic agent that is actively accumulated by platelets.