FREE COMMUNICATIONS XVI

Platelets: Control and Interactions.

THE CONTROL OF PLATELET FUNCTION BY CYCLIC AMP AND THROMBOXANE SYNTHESIS. N.U. Bang, M.G.J. Boxer, R.O. Heidenreich, P.P.K. Ho, and M.J. Schmidt. Lilly Research Laboratories; V.A. Hospital; Department of Medicine, Indiana University, Indianapolis, Indiana, U.S.A.

Platelet (P) levels of cyclic AMP (cAMP) and thromboxane (TX) synthesis have been identified as major regulators of P aggregation and release. We have utilized as probes drugs which either decrease TX synthesis by cyclooxygenase inhibition (aspirin and indomethacin) or which increase P cAMP (adenosine; PGE_1; theophylline; isobutylmethylxanthine; and SH-869, a dipyridamole analog) to evaluate relative contributions of cAMP and TX and their possible interreactions in mediating P function. Cyclooxygenase inhibitors at concentrations 8-16 fold lower than those inhibiting P aggregation and release caused almost complete inhibition of TXB_2 synthesis from exogenous ^{14}C-arachidonic acid (aa) and malonyldialdehyde (MDA) production in P stimulated by thrombin (T) or N-ethylmaleimide (NEM). Drugs elevating P cAMP at concentrations equal to or greater than those causing complete inhibition of P aggregation and release did not inhibit TXB_2 synthesis from exogenous ^{14}C-aa, nor did they inhibit MDA production in P stimulated by NEM or by concentrations of T sufficient to produce maximal TX synthesis. However, these drugs variably inhibited MDA production when P were stimulated at lower T concentrations causing only minor TX synthesis. Thus, elevated P cAMP did not inhibit TX synthesis from aa but appeared to weakly inhibit aa phospholipase. We conclude that TX synthesis cannot be the sole, final mediator of P aggregation and release but that these events result from as yet unidentified mechanisms modulated largely independently by TX synthesis and intra-P cAMP levels.

CALCIUM BINDING SITES ON HUMAN BLOOD PLATELETS. S. Heptinstall. University Department of Medicine, General Hospital, Nottingham, England.

Extracellular calcium ions are required for platelets to aggregate in response to various aggregating agents. Although magnesium ions can sometimes stimulate aggregation they only do so when a small amount of calcium is present. The calcium bound to washed human platelets suspended in buffered saline containing 0-200μM $^{45}CaCl_2$ depends upon the extracellular calcium concentration. Scatchard analysis of the binding data suggests that a few (0.8×10^6) relatively high affinity ($K = 85,000$) calcium binding sites are present on each platelet. When 2.5mM $MgCl_2$ is included in the saline suspensions the calcium bound to the platelets is only reduced at the higher calcium concentrations. Magnesium ions do not displace the tightly bound calcium. It is suggested that these specific calcium binding sites are involved in platelet aggregation.