POSTER SYMPOSIUM I

Platelets: Prostaglandin Synthesis.

UNIQUE SIGNIFICANCE OF DIHOMO- γ -LINOLENIC ACID MECHANISMS FOR THE PREVENTION OF THROMBOSIS. A. L. Willis, Roche Products Ltd., Welwyn Garden City, England.

Common anti-platelet aggregatory agents act like aspirin to block cyclo-oxygenation of arachidonic acid (AA) to the endoperoxide PGH_2 . Alternatively, they act like PGE_1 to increase platelet cyclic AMP (cAMP). Inhibition of platelet production of thromboxane (TX) $_2$ may also be desirable. Dihomo- γ -linolenic acid (DHHA) apparently acts through these and other mechanisms. Competition of DHHA with AA for vesicular gland cyclo-oxygenase occurred so that anti-aggregatory PGE_1 and PGI_2 were produced at the expense of PGH_2 and PGE_2 (which together produce aggregation); O_2 uptake was unimpaired. Consistent with such an action in platelets, the anti-aggregatory effects of DHHA were prevented by aspirin or other inhibitors of cyclo-oxygenase and were enhanced by Ro 21-1724, a selective inhibitor of cAMP phosphodiesterase. Prior incubation of platelet microsomes with DHHA suppressed conversion of AA to a TXA_2 -like vasoconstrictor substance and to more stable material behaving like TXB_2 on radio-TLC. In addition, DHHA may compete with dietary AA for incorporation into PG precursor pools. The multiple mode of action reported here supports a concept that DHHA is a natural anti-thrombotic factor of key importance.

LECITHIN ANALOG AS A NEW PLATELET AGGREGATING AGENT. J. Hawiger and H.W. Hooper, Jr., Vanderbilt University and VA Hospital, Nashville, Tennessee, USA.

Lecithin comprises 32% of the human platelet phospholipids which are the source of arachidonic acid required for biosynthesis of prostaglandin endoperoxides, potent inducers of platelet aggregation. A synthetic analog of lecithin, dimethyl-DL-2,3-distearoyloxypropyl-2'-hydroxyethylammonium acetate known as a phospholipase A inhibitor, showed a profound in vitro effect upon human platelets. Blood platelets obtained from normal, healthy, fasting volunteers and suspended in autologous plasma aggregated in response to lecithin analog. Platelet aggregation was dose-dependent within the range of 10^{-5} to 10^{-4} M of lecithin analog and accompanied by release of [^3H]serotonin. In contrast, addition of equimolar or higher amounts of lecithin to human platelets in vitro remained without a measurable effect on their function. Sensitivity of human platelets to the lecithin analog used was increased at least 10-fold by separation of platelets from the bulk of plasma proteins by gel filtration on Sepharose 2B. Release of [^3H]serotonin from gel-filtered platelets induced by the lecithin analog studied was dose-dependent and partly reversible due to reuptake of serotonin. Thus, the lecithin analog used in our experiments is a new platelet activating agent which is a "false phospholipid" and phospholipase A inhibitor acting through a previously unrecognized mechanism triggering membrane-mediated functions of human platelets.