INHIBITION OF PLATELET AGERGATION BY BRINOLASE DEGRADATION PRODUCTS OF FIBRINOGEN AND SERUM ALBUMIN. M.H.E. Roschulak. Department of Pharmacology, University of Toronto, Toronto, Canada.

Brinolase (fibrolytic enzyme from Aspergillus oryzae) was observed to possess significant platelet aggregation inhibitory properties during and after thrombolytic therapeutic use. These platelet effects were found in vitro to be caused in part by intermediate products of fibrinogen digestion, namely low-molecular-weight peptides of approx. MW 2500. Human fibrinogen peptides were isolated, purified, and shown to have high inhibitory activity in platelet-rich plasma. Quantitative comparisons of attainable platelet inhibition in vitro and observed responses in vivo during administration of equivalent enzyme doses, however, suggested that total available fibrinogen, even if it were entirely converted to degradation products (which it is not), would be insufficient to account for observed platelet effects of brinolase therapy.

Human serum albumin is also readily degraded by brinolase. Albumin degradation products were prepared in vitro by optimal incubation with the enzyme. Dose-response curves of inhibition of platelet aggregation were obtained with lyophilized peptides in platelet-rich plasma in vitro, and significant inhibition of platelet aggregation was observed in vivo following infusion of albumin degradation products into rabbits. The enzyme doses and amounts of substrates employed in all experiments were equivalent to the conditions of therapeutic fibrinolysis. Thus, albumin degradation products are considered to contribute a significant, if not the major, portion of platelet-active intermediates during clinical brinolase therapy. Albumin cleavage, which is unique to brinolase amongst clinical fibrinolytic enzymes, was shown to have biological effects of its own, but it may also serve to protect coagulation proteins from enzymatic destruction through competition for the enzyme during systemic brinolase therapy.

BLOOD PRODUCT INFUSIONS TO MAINTAIN NORMAL HEMOSTASIS PARAMETERS IN LOW BIRTHWEIGHT INFANTS. J.M. Cash and T.L. Thom. Blood Transfusion Centre, Royal Infirmary, Edinburgh, Scotland.

Hemostatic parameters were measured serially for 3 days in 36 infants, within 2 hours of birth. Twelve (21%) maintained normal coagulation profiles, whereas 46 (79%) had abnormal profiles. The abnormal group were randomly allocated to a control (23) and treatment subgroup (23). Treatment consisted of infusions of platelets, fibrinogen (cryoprecipitate) and/or factor II, V, VII, IX & X concentrates - whichever was appropriate, and repeated when necessary.

The results revealed a lower incidence of intraventricular hemorrhage in the treated subgroup, but this was not statistically significant. There was no difference in mortality between the two subgroups. No deleterious effects due to the administration of blood products; in particular, DIC or local thrombosis was not observed.

It is concluded that although efforts to maintain normal hemostasis in these high risk neonates are possible and may be safe, they are without demonstrable benefit.


H Continental Pharma, Research Laboratories, Brussels, Belgium.
H Institut Médico-Chirurgical d'Anderlecht (service du Dr Hacq), Brussels, Belgium.
H Laboratory of Blood Coagulation (Prof. Dr. M. Verstraete) Medical Research Dept. Academisch Ziekenhuis St. Raphaël, University of Leuven, Leuven, Belgium.

Several methods have been proposed for the determination of platelet life-span. Among them the technique described by Stuart et al (1) based upon the ex-vivo assay of platelet malondialdehyde after one single oral intake of acetyl salicylic acid is receiving an increasing interest. We adapted this method for semi-automated determinations using an Autoanalyzer system.

Platelet survival time was determined with this technique in healthy volunteers as well as in patients with abnormal platelet life-span.

In some instances chromium-51 determinations were also performed in order to assess the reliability of the method proposed. The results obtained are comparable for both methods and compatible with those described in the literature.