

DISCOCYTE-ECHINOCYTE TRANSFORMATION IN HUMAN PLATELETS: GEOMETRIES OF ECHINOCYTES PREPARED WITH OSMOTIC STRESS AND AGGREGATING AGENTS. John G. Milton and M.M. Frojmovic. Department of Physiology, McGill University, Montreal, Canada.

Many agents cause platelets in the disc-form (discocytes) to change into spherical forms from which many pseudopods project (echinocytes). It is not known whether echinocytes prepared with different stimuli are the same. Here we investigate the geometries of echinocytes prepared with aggregating agents and osmotic stress. Geometric parameters were estimated from a cinematographic analysis of freely-rotating platelets in citrated platelet-rich plasma (PRP) under a phase contrast microscope. Echinocytes were prepared by the addition of adenosine diphosphate, thrombin or 35-50% by volume of distilled water to PRP. Under conditions of osmotic stress, 75-90% of the discocytes convert to echinocytes within five minutes followed by a slow reversion to discocytes complete within 1 - 2 hours. Main body diameters for the echinocytes, excluding consideration of the pseudopods, were in all cases  $2.1 \pm 0.4$   $\mu$ m. Comparisons of the mean volume and mean surface area of the main body of the echinocyte with that of the original discocyte show that in each case echinocyte formation is accompanied by: 1)  $\sim 15\%$  reduction in main body platelet volume, and 2)  $\sim 25\%$  decrease in main body platelet surface area.

These results indicate that the main body geometries of echinocytes are essentially independent of the stimuli used and suggest a common pathway for echinocyte formation with  $\sim 1/4$  of the original discocyte surface area available for pseudopod formation.

Generation of Fibrinogen Degradation Products (FDP's) by Neutral Proteases from Human Granulocytes and their Importance for the Blood Clotting System.

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The effect of neutral proteases from human granulocytes (elastase-like and chymotrypsin-like protease) on purified human fibrinogen was investigated. Detectable by two-dimensional and polyacrylamide electrophoresis, dependence of fibrinogen degradation of enzyme concentration and incubation time was found. Molecular weight of the FDP's was estimated by gelchromatography. Some greater FDP's showed the antigenic determinants of fibrinogen and of the split products D and E. High molecular weight FDP's inhibited fibrinogen clotting. Generated at high enzyme concentrations and longer incubation times, FDP's lost their ability to clot themselves and to interfere with fibrin polymerization.

As these fibrinogen degrading enzymes are released by the influence of antigen-antibody-complexes and endotoxine, it can be assumed that clotting defects in patients with acute leukemia, septicemia a. o. are caused by the effects of the proteases on fibrinogen and the accumulation of FDP's.

ANTITHROMBIN III AND HYPERCOAGULABILITY IN SMOKERS. R. Losito, D. Nathan, H. Gattiker and B. Longpré. Centre Hospitalier Universitaire, Sherbrooke, P.Q., CANADA.

It is known that various coagulation tests such as the thromboplastin generation test (TGT), thrombin generation (TG), levels of factor VIII or antithrombin III have been found to be abnormal in individuals with intravascular coagulation or having an increased tendency to thrombosis. The aim of this study was to evaluate the role of the TGT, TG, factor VIII and antithrombin III assays in the diagnosis of possible mild intravascular coagulation in patients undergoing cardiac catheterization who had a history of smoking. In addition to these four tests, a routine coagulogram was performed for a total of 13 tests. It appeared that smokers had more abnormal tests (7.3/patient) than the controls (3.3/patient). The greatest association was between TGT and TG (29.6%) and TG and AT-III (25.9%). If by definition, hypercoagulability is present where 3 or more of these 4 mentioned tests were abnormal, then five patients were found to be in this category; all, except one, formed clots. In the patients (50) with a history of smoking, a third were found to have the TGT and the TG abnormal; however, the most striking observation in this group was in the antithrombin III where it was noted to be low in forty-five percent of the patients compared to the controls (patients having catheterization and were non-smokers) whose antithrombin III was found to be decreased in only five percent of the individuals. It is concluded that determination of antithrombin III may be of more importance in assisting the detection of hypercoagulability, especially in the smoking population, than the TGT, TG, or factor VIII.