cannot observe a release of heparin-neutralizing activity (PF4) and adenine nucleotides, an activation of clot-promoting activity (PF3), or a significant uptake of $^{45}$calcium into platelets. Electron micrographs of platelets after exposure to X-537A do not exhibit the alterations known to be coupled with the release reaction, despite a considerable release of serotonin. Two-phase partition studies demonstrate that X-537A is able to extract serotonin into an organic phase. In summary, these results indicate that X-537A causes a selective release of serotonin by transporting it through membranes. Only at high concentrations of X-537A can one establish an uptake of $^{45}$calcium by platelets and a release of PF4 and adenine nucleotides in addition to that of serotonin.

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*F. A. Belamarich* (Boston University, Bonston, Massachusetts 02215, U.S.A.): **The Effect of Reserpine on Aggregation of Avian Thrombocytes. (135)**

Avian nucleated thrombocytes are aggregated by acid-soluble collagen, and serotonin (5-hydroxytryptamine) is released from the thrombocytes during the process of aggregation. The action of collagen is inhibited by aspirin and methysergide, a serotonin antagonist. Exogenous serotonin can also induce aggregation. These observations suggest that serotonin, which has been shown to be stored in avian thrombocytes, acts similar to released ADP in mammalian platelets.

Measurement of serotonin content in the blood of Peking ducks *(Anas platyrhynchos)* which had been given reserpine (3 mg/kg, blood withdrawn 20 hours after injection) showed that the serotonin content of whole blood and thrombocyte-rich-plasma fell to approximately 90 percent of the control level. Analysis of aggregation of thrombocytes from control and reserpinized ducks showed that reserpinization markedly decreased aggregation induced by collagen, while it enhanced aggregation induced by serotonin. These results are consistent with the concept of released serotonin playing a role in thrombocyte aggregation.

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*F. Heřmanský, P. Cieslar, O. Matoušová and K. Smetana* (Ist Medical Clinic, Charles University, 12808 Prague 2, ČSSR): **Study of Albinism in Relation to Heřmanský-Pudlák Syndrome. (136)**

Up to now 24 patients with oculocutaneous albinism have been investigated in this study to find out the frequency of characteristic signs of HPS. Seven of them suffered from mild bleeding tendency. Platelet defects of storage pool disorder type have been revealed at a varying degree in all these cases. (Aggregation abnormalities, decrease of total platelet ADP contents and of its release, lower serotonin uptake with the lack of very dense bodies in ultrathin sections). This thrombocytophathy has been regularly associated with the storage of pigment typical for HPS in their bone marrow. In 7 of 17 remaining albinos with normal platelet functions some increase in the accumulation of non-specific cytochemically different lipopigments was noted.

Our results demonstrate a rather frequent occurence of HPS in albinos and suggest a mutation of one common gene or of closely linked genes as a cause of complete HPS.

*J. G. White, J. M. Gerrard, G. H. R. Rao, J. R. Edson and C. J. Witkop* (University of Minnesota, Minneapolis, Minnesota): **Differences in Platelet Storage Pool Deficiency (SPD) of Hermansky Pudlak Syndrome (HPS) and Non-Albinos (NA). (137)**

Recent reports of SDP platelets from patients with HPS (Albinism, accumulation of ceroid-like pigment, and mild hemorrhagic disease) and NA have suggested that the platelet defect in both conditions is identical. However, investigation of six HPS patients and three NA siblings with platelet SPD have indicated significant differences. The three NA patients were mildly thrombocytopenic while HPS patients had normal platelet counts. Levels of platelet serotonin (5 HT) were consistently lower in HPS than in NA with SPD, and

approached normal concentrations in 2 of 3 NA patients. Dense bodies (DB), the organelles which contain the storage pool of serotonin and adenine nucleotides, were virtually absent in HPS platelets. SPD platelets from NA patients had significant numbers of DB which were markedly abnormal in their ultrastructure compared to normal platelet DB. Analysis of lipid peroxides and other substances reacting with thiobarbituric acid (TBA) revealed levels 5 to 10 times normal in HPS platelets while concentrations in SPD platelets from NA patients were similar to control values. Although the bleeding problems, aggregation defects, and abnormal platelet adenine nucleotide profiles were similar in HPS and NA patients, results of this study suggest that basic differences exist. The bizarre appearance of dense bodies in NA platelets is compatible with a structural abnormality interfering with storage organelle formation while accumulation of TBA reactive substances by HPS platelets may be the critical factor preventing development of the storage pool.

*F. Pareti, A. Capitanio, V. Chantarangkul and P. M. Mannucci* (Haemophilia and Thrombosis CTR – University of Milano, Itlay): **Acquired Storage Pool Deficiency in Platelets during DIC.** **(138)**

During DIC, circulating platelets are exposed to thrombin and other aggregating agents causing the release reaction. It is conceivable that "stimulated" platelets may have altered functions which contribute, with the decrease in number, to the bleeding tendency of these patients. Platelet aggregation, adenine nucleotides (AN) content and release, serotonin (5 HT) content, uptake and metabolism have been investigated in a patient with an acute bleeding tendency associated to laboratory findings suggesting the occurence of DIC. Secondary aggregation to ADP and adrenaline was absent; collagen aggregation was also defective. Release of AN induced by different collagen concentrations was much lower than in the normal controls. Levels of AN were reduced (mainly ADP); ATP/ADP ratio was higher than in control platelets. Since AN of the metabolic pool were normal, the deficiency is due to lack of AN of the storage pool. 5 HT content and the ability to take up the exogenous amine was also reduced in the patient' platelets. Their prolonged incubation with 14 C 5 HT resulted in a progressive loss of radioactivity in plasma, while normal platelets, in the same conditions, stored the amine throughout the incubation period. This abnormal behaviour has been observed in platelets of patients affected by congenital storage pool deficiency (SPD) and is caused by abnormal platelet metabolism of the amine. The abnormalities observed in this patient with DIC are stikingly similar to those present in congenital SPD and are likely to be produced by in vivo exposure to aggregating agents followed by release of storage granules.

*L. Poller and Jean M. Thomson* (Department of Haematology, Withington Hospital, University Hospital of South Manchester, Manchester M20 8LR Great Britain): **The Effects of Natural Oestrogens on Blood Clotting.** **(139)**

A double-blind cross-over trial on natural conjugated oestrogens (Premarin) has been conducted in women volunteers. Base-line studies were performed on blood clotting and platelet function and these were repeated at 3 month intervals during therapy. Laboratory results and possible thrombogenic implications are discussed.

*G. I. C. Ingram* (St. Thomas' Hospital and Medical School, London SE1 7EH, England): **ICSH-ISTH International Anticoagulant Control Study III. Implications of the Findings.** **(140)**

For general standardization of oral anticoagulant control, the results of tests performed with the present diversity of reagents must be referable to a common scale. To date, most comparative work has been related to the relative sensitivities of different thromboplastins to the anticoagulant defect. A "master" reference thromboplastin, against which working reference materials – thromboplastins and standardized plasmas – could be expertly calibrated, may well provide the backbone of an international scheme. For working laboratories, anticoagulant treatment could then be controlled by using either a thrombo-