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EFFECT OF PREDNISONE ON PLATELET FUNCTION IN PATIENTS WITH BLEEDING DISORDERS. R. McKenna, *F. Bachmann, O. Pichairut and B. Whittaker. Section of Hematology, Rush-Presbyterian St. Luke's Medical Center, Chicago, IL., U.S.A. (*Current Address: Laboratories Central d'Hematologie, Lausanne, Switzerland).

There is considerable controversy regarding the effect of Prednisone on the hemostatic mechanism of normal people versus patients with bleeding diatheses. We administered Prednisone 15 mg TID to patients with a positive history of a bleeding disorder, and evaluated the bleeding time and other in-vitro tests of platelet function prior to and between the 5th and 7th day after Prednisone.

Eleven patients were admitted into this study over a one year period. All patients had a history of excessive bruising, epistaxis, bleeding after dental extractions, and gastrointestinal or other bleeding in various combinations. Two out of the eleven had template bleeding times of greater than 15 minutes both before and after the Prednisone. These two patients were subsequently proven to have von Willebrand's disease by the washed platelet ristocetin assay. In the remaining 9 patients, the pre-Prednisone bleeding time was 9.3 $\pm$3.7 minutes ($\bar{x}$ $\pm$1 S.D.) whereas the post-Prednisone bleeding time was 5.8 $\pm$3.6 minutes ($\bar{x}$ $\pm$1 S.D.). These results were significant(t_d=3.83;d_f:7;p=0.007).

Platelet aggregation in response to exogenous ADP (1 μM, 3 μM) Sigma bovine tendon collagen (1.8 mg/ml F) and epinephrine (5.5 x 10^{-4}M), platelet retention in a glass bead column or platelet factor 3 availability did not improve or worsen after Prednisone therapy. The mean platelet count of 328,000 $\pm$94,000 ($\bar{x}$ $\pm$1 S.D.) was significantly (p=0.05) higher than the mean pre-Prednisone platelet count of 268,000 $\pm$77,000 ($\bar{x}$ $\pm$1 S.D.).

In conclusion, we have shown that large doses of Prednisone appear to shorten the bleeding time in patients with significant defects in the primary hemostatic mechanism. However the bleeding time improvement is not evident in patients with von Willebrand's disease.

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HEPARIN RESISTANCE IN THROMBOCYTOSIS AND ERYTHROCYTOSIS. T. Wajima and T. R. Maloney. Department of Hematology-Medical Oncology, Wilford Hall USAF Medical Center, San Antonio, Texas.

Heparin is generally considered to be the drug of choice in the treatment of venous thromboembolism. In most patients an adequate anticoagulant effect can be achieved with doses between 20,000 and 30,000 units/24 hrs. Increased heparin requirement or "resistance to heparin treatment" is seen in patients with massive deep vein thrombosis (DVT), pulmonary emboli, severe AT-III deficiency, or some cancer patients. We encountered heparin resistance in 7 patients, 3 with idiopathic thrombocytosis and 4 with recurrent CVA's and DVT associated with relative erythrocytosis. In these patients, a therapeutic prolongation of APTT was not achieved by usual doses of heparin, and thromboembolic episodes occurred despite administration of heparin in doses sufficient to prolong APTT to the therapeutic range. The initial PT, PTT, and TT in these patients were normal. Protamine Sulfate test and Ethanol gelation test were negative. Fibrinogen and Factor VIII levels were elevated in all patients. AT-III levels (by immunodiffusion method) were normal. Liver and renal function tests were normal. In the patients with idiopathic thrombocytosis, platelet counts were over 1,500 x 10^9/l. Platelet aggregation by ADP, epinephrine and collagen was normal or slightly increased. Patients with idiopathic thromocytosis were treated with nitrogen mustard and/or busulfan to reduce the platelet count, then treated with heparin.

Patients with relative erythrocytosis had elevated Hct (>55), Hgb (>18 gm%) and whole blood viscosity (>6 with normal <4), but normal red cell mass; plasma volumes were markedly decreased. Platelet counts were normal to slightly increased. Platelet aggregation studies were normal. These patients were treated with hydration and plebotomy to reduce the Hct below 45 and restore normal whole blood viscosity, then with heparin with good clinical results. Correction of thrombocytosis and erythrocytosis is important in optimal anticoagulation.

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BETA - THROMBOGLOBULIN AND HA - PLATELET FACTOR 4 IN MULTIPLE MYELOMA, HODGKIN DISEASE AND MALIG - NANT LYMPHOMA - EFFECTS OF THERAPY. H.-G. Klingemann, R. Egbring and K. Havemann Department of Internal Medicine, University of Marburg, West - Germany

Determination of platelet specific proteins Beta-Thromboglobulin (β-TG) and High Affinity Platelet Factor 4 (PF 4) in plasma has been proved as useful marker for an enhanced release reaction in some diseases, mostly due to an in - creased platelet aggregation. To evaluate suit - able marker for a prethrombotic state in some myeloproliferative diseases we investigated pa - tients suffering from multiple myeloma, Hodgkin disease and malignant lymphoma. β- TG and PF 4 were measured in platelet poor plasma using RIA - kits (Amersham-Buchler / Abbott Labor.). In addition we determined: platelet count, spontaneous and collagen induced platelet aggregation, the activity of AT III and of the clotting factors I,V,VIII,XIII and the concentration of FDP. RESULTS: Normal range was found to be o-55 ng/ml for β-TG and o-12 ng/ml for PF 4. Both release proteins were increased in 17 out of 25 patients with myeloma, in 13 out of 15 patients with Hodgkin disease and in 1o out of 12 patients with malignant lymphoma. A correlation to the severity of the diseases were demonstrable. Chemotherapy caused a decrease of β-TG and PF 4 levels in some cases. However no correlation could be found between β- TG and PF 4 levels and in vitro tests of platelet aggregation. Further clotting assay provided evidence for an activation of clotting (like DIC) in a few patients. Other possibilities - like the release of the platelet specific proteins by immunocomplexes, prostaglandins or proteolytic enzymes from granulocytes must taken into account.

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A RADIOIMMUNOASSAY FOR THE QUANTITATION OF BOVINE PLATELET FACTOR 4 AND ITS USE IN MONITORING ARTIFICIAL HEART IMPLANTS D. M. Clark, J. Deneris, E. F. Workman, Jr., D. Olsen. Abbott Laboratories, North Chicago, Illinois, U.S.A. and University of Utah, Division of Artificial Organs, Salt Lake City, Utah, U.S.A.

A radioimmunoassay for the quantitation of bovine platelet factor 4 (PF4) has been developed for use on bovine plasma. The assay utilizes classical radioimmunoassay techniques; 50λ of standard or plasma are mixed with 250λ ^{125}I-bovine PF4 and 250λ goat anti-bovine PF4 for two hours at room temperature. Antibody-bound PF4 is separated from free PF4 by precipitation with ammonium sulfate. The resulting standard curve has a least detectable dose of 50 ng/ml, a 50% intercept around 400 ng/ml, a range of 0-1000 ng/ml and is unaffected by the presence of heparin in samples. Plasma samples are collected using a two-Vacutainer technique employing Thrombotect^{TM} collection tubes (Abbott Laboratories) which have been developed to minimize any in vitro platelet release. The mean PF4 concentration of 7 healthy control calves was 55 ng/ml with a range of 0 to 180 ng/ml. PF4 levels were measured serially in calves which had undergone artificial heart implantation.

In one calf with a pre-operative PF4 level of 99 ng/ml, the PF4 level increased to 638 ng/ml during post-surgical complications 7 days after surgery and subsequently decreased to 230 ng/ml after coumarin therapy 27 days after surgery. A similarly implanted calf without post-surgical complications had a pre-operative PF4 level of 180 ng/ml and a 20 day post-surgical level of 245 ng/ml. These data suggest that PF4 levels are elevated in post-surgical hypercoaguable states and that measuring PF4 provides a useful tool for monitoring the post-surgical patency of artificial surfaces such as prosthetic valves, artificial hearts, left ventricular assists and thoracic surgery in general. This program is under further investigation to increase the understanding of platelet involvement in such systems, to determine how long PF4 elevations exist prior to the onset of clinical symptoms and to follow the success or failure of anticoagulant therapies.