EVALUATION OF IN VIVO PLATELET ACTIVATION IN SICKLE CELL DISEASE. J.F. Watson-Williams, J. Westwick, S. Krishnamurthi, G. Marks, J. White and V.V. Lakkak. Thrombosis Research Unit, Rayne Institute, King's College Hospital, London, England.

This study was made to identify indicators of in vivo platelet activation in patients with sickle cell disease. Seven patients, homozygous for sickle cell haemoglobin and seven age, sex and race matched controls were each studied 2 or 3 times in a six week period of normal health. Venous blood was drawn with minimal use of a tourniquet and, after platelet activation in patients with sickle cell disease.

Hematology

Blood was taken for other tests, 2.5ml was collected into ice-cold "Hansham BTG" tubes. The samples were centrifuged at 2,600g for 25 minutes at 0°C and the plasma immediately separated and stored at -20°C until assayed for Betathromboglobulin (BTG), platelet factor 4 (PF4), Thromboxane (TxB2), and 6-oxo-PGF1α. Circulating platelet aggregation was measured by the method of Wu and Hoak (1974).

BTG was greater than 60% in 17 of 20 samples from the patients but in only 4 of 17 samples from the controls. This difference remained significant when corrected for the platelet count. In vivo aggregation was above 25% on 8 of 16 occasions in patients and on 3 of 16 occasions in controls. Plasma PF4, TxB2, and 6-oxo-PGF1α levels were not significantly different in the two groups. BTG and in vivo platelet aggregation may be useful parameters with which to assess platelet in vivo platelet activation in patients with homozygous sickle cell disease whilst not in crisis.

Mean Values

| BTG ng/ml plasma | 42 | 90 | <.0001
| 6-oxo-PGF1α | 0.3 | 0.4 | .03
| PF4 ng/ml plasma | 14.3 | 24.5 | <.002
| ng/10^9 platelets | 24 | 35 | .1
| TxB2ng/ml plasma | 9.0 | 8.0 | N.S.
| TXB2-Ag/ml plasma | 67.4 ± 18.2 | N.S.
| 6-oxo-PGF1α | 0.24 | 0.20 | .3
| in vivo platelet aggregation | 13.2 | 30.0 | <.02

* Statistical Analysis by Mann and Whitney U Test.
* Figures are measurable values and total samples tested.

CHANGES IN MEMBRANE PHYSICOCHEMICAL PROPERTIES OF HYPERREACTIVE PLATELETS IN ESTROGEN-TREATED PROSTATIC CANCER. S. M. Jung, T. Isohisa, K. Kinoshita, and H. Yamazaki. Division of Cardiovascular Research, The Tokyo Metropolitan Institute of Medical Science and Department of Urology, Komagome Metropolitan Hospital, Tokyo, Japan.

Aggregation and physicochemical properties of platelets from 5 prostatic cancer patients, 20 prostatic cancer patients, 300 mg stilbestrol diphasate/day (0.5% of patients), 16 of the same patients given 300 mg aspirin/day, 19 prostatic hyperthropy patients, and 19 males were examined. Prostatic cancer on estrogen showed higher platelet aggregability towards ADP, adrenaline, and collagen than the other groups tested. Mean platelet electrophoretic mobilities were determined by the automatic Laser Zee 3000 system and the value for prostatic cancer on estrogen was <1.534 ± 0.865, 1.526 ± 0.009, and 1.533 ± 0.012 um/sec/V/cm respectively. Electrophoretic mobility was a linear function of whole platelet stalic acid (r=0.96, p<0.05). The result suggests that the electrophoretic mobility of platelets was defined by sulic acid amount and there may be a selective consumption of platelets with less surface negative charge in prostatic cancer on estrogen. Membrane glycoprotein patterns determined by SDS-polyacrylamide gel electrophoresis showed prostatic cancer on estrogen to have lower glycoprotein I and higher glycoprotein IV than other groups (p<0.05). There may be factors affecting changes on platelet membranes or population in such patients. Prostatic cancer on estrogen decreased platelet mobilities in 14 out of 16 cases with loss of linear relationship between mobility but no changes on sulic acid or glycoprotein pattern from those before medication of PF4 with aspirin resulted in dose dependent increase in mobility with concomitant aggregability loss. The effect suggests another kind of inhibitory mechanism on platelet aggregation in addition to cycloxygenase inhibition.

FIBRINOGEN PROTEOLYSIS AND PLATELET ACTIVATION IN MYELOPROLIFERATIVE DISORDERS. H. Ireland, D. A. Lane, S. Wolff and G. D. Peggarn. Department of Haematology, Charing Cross Hospital and Medical School, London, U.K.

We have studied 18 patients with myeloproliferative disorder to determine whether their abnormal platelet function and increased plasma 6-thromboglobulin (6-TG) are associated with activated coagulation and fibrinolytic systems. Of these patients, 6 had polycythaemia rubra vera, 8 had myelofibrosis and 2 had thrombocythaemia. We measured plasma concentrations of the thrombin sensitive fibrinopeptide A (FPA), the plasmin sensitive fibrinogen fragment B 81-42, and 8 TG by radioimmunoassay. We also studied platelet aggregation in response to ADP. Mean normal values (n = 20) for FPA, B 81-42 and 8 TG were 1.06, 1.59 and 0.80 pmol/ml respectively. The 18 patients showed minimal plasma thrombin and plasmin activities with a disproportionately large platelet release. Mean FPA, B 81-42 and 8 TG levels were 1.74, 3.31 and 3.12 pmol/ml, respectively. These patients exhibited increased, decreased and normal platelet aggregation but no specific defect was associated with any particular radioimmunoassay result. 5 of these patients, 4 of whom had increased aggregation were treated with aspirin in sufficient doses to eliminate their secondary response to ADP. FPA and B 81-42 were not altered but 8 TG was reduced from 3.93 to 2.72 pmol/ml. We also studied 10 patients with idopathic thrombocythaemia. These patients showed minimal plasma response to ADP. Their FPA, B 81-42 and 8 TG levels were similar to normal, 0.7, 1.93 and 0.97 pmol/ml respectively. We conclude that in myeloproliferative disorders (a) increased plasma concentration of 8 TG is not associated with a particular platelet aggregation abnormality (b) in the majority of patients the increased 8 TG level is not a consequence of thrombin action (c) the raised FPA and 8 81-42 plasma levels in the minority of patients cannot be attributed solely to increased red cell mass (d) much of the 8 TG release is probably independent of the cycloxygenase pathway.