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EVALUATION OF PLATELET REACTIVITY IN PATIENTS WITH ABNORMAL HEART VALVES. J.M. Riddle, D.J. Magilligan and P.D. Stein. Departments of Internal Medicine and Surgery, Henry Ford Hospital, Detroit, Michigan, USA.

The reactivity of platelets from 57 patients was evaluated prior to removal of either an abnormal natural mitral or aortic valve or a degenerated porcine bioprosthetic valve. Thirty patients had aortic stenosis or insufficiency, 21 had mitral stenosis or insufficiency, and 6 underwent the removal of a long-term (4 to 7 years after insertion) Hancock porcine bioprosthetic valve. Transmission electron microscopy was used in a standardized in vitro method to evaluate these platelets. The degree of surface activation (cytoplasmic spreading by single platelets) and aggregate formation were both recorded. A hyperactive response was defined as >20% of the spread type platelet and/or an increased number of aggregates (>93 aggregates/100 single platelets). Hyperactive platelet populations were found in only 8% (6 of 72) of normal subjects. In contrast, 60% (18 of 30) of patients with aortic stenosis or insufficiency, 76% (16 of 21) of patients with mitral stenosis or insufficiency, and 83% (5 of 6) of patients with a degenerated porcine valve showed hyperactive platelets. The mean percentage of the spread type platelet for the various groups was 40, 38 and 30 respectively with corresponding mean values of 106, 124 and 102 for platelet aggregates. The reactivity of platelets from the normal group differed significantly from each group of patients with abnormal valves ($P < 0.01$). However, the level of platelet reactivity between the patient groups with abnormal valves did not differ significantly. Disturbed flow, high shear stresses and the exposure of potentially thrombotic materials are all features associated with abnormal natural heart valves as well as a degenerated bioprosthesis and may explain our finding of increased platelet reactivity in these patients.

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VESSEL INJURY, THROMBOSIS AND PLATELET SURVIVAL. P.D. Winocour, M. Cattaneo, R.L. Kinlough-Rathbone and J.F. Mustard. McMaster University, Hamilton, Ontario, CANADA.

In vascular disease it is unclear whether shortened platelet survival (PS) primarily reflects vessel injury or thrombosis. In rabbits and rats (4-6 animals per group) we examined the relations among experimental thrombosis, vessel wall injury and platelet survival and turnover. In rabbits preinjected with autologous ^{51}Cr-platelets, a 20 cm intra-aortic-catheter in situ for 4 days resulted in a thrombus (mean wt. 23.4 mg). A significant amount of ^{51}Cr was associated with the aorta (0.53 ± 0.13% of total ^{51}Cr circulating before surgery). PS was reduced (no catheter 62.4 ± 8.8; catheter 37.0 ± 5.6 hr, $p<0.05$). With a 10 cm catheter, thrombus wt. was similar (mean 24.0 mg). ^{51}Cr associated with the aorta was 0.25% ± 0.06% but PS was unaffected (no catheter 55.4 ± 6.8; catheter 53.8 ± 3.6 hr). In other experiments, sham-operated controls were compared with rabbits with 20 cm catheters. Mean thrombus wt. was 30.2 mg and 0.53 ± 0.11% of the ^{51}Cr was associated with the aorta. PS was significantly shorter in the catheter rabbits (36.7 ± 2.8 hr) vs sham-operated controls (68.0 ± 10.4 hr, $p<0.02$); platelet turnover was significantly increased (14,500 ± 970 vs 9,950 ± 1,020 per mm^3/hr, $p<0.01$). Three groups of rats preinjected with homologous ^{51}Cr-platelets were studied: a) sham-operated, b) aortic catheter 7.5 cm, c) aortic catheter 12.5 cm. No macroscopic thrombi were observed at any time during the 4 days that catheters were in situ. Mean PS was: a) 97.7 ± 2.4, b) 88.5 ± 2.6 and c) 63.7 ± 5.1 hr ($p<0.001$, a vs c). Platelet turnover was a) 8,400 ± 720, b) 8,900 ± 870 and c) 11,000 ± 1,150 per mm^3/hr. ^{51}Cr associated with the aortae was a) 0.004 ± 0.001, b) 0.013 ± 0.006 and c) 0.027 ± 0.011% of total ($p<0.05$, a vs c). Thus in rats, catheters shorten PS without thrombosis. Therefore, with catheter-induced vessel injury PS appears directly related to length of catheter and extent of injury. Shortened PS can occur without thrombus formation and thrombus formation can occur without changing PS or platelet turnover.

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DECREASED PLATELET SURVIVAL AND AGGREGATION IN MICE EXPOSED TO HYPOBARIC HYPOXIA. C.W. Jackson, M.A. Whidden, P.J. Smith, C.C. Edwards and S.A. Lyles. Division of Hematology/Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee 38101

Decreased platelet survival and function have been observed in patients with chronic hypoxemia. To develop a model for investigating these problems, we have studied the mouse exposed to severe hypobaric hypoxia. Mice were exposed to 0.3 or 0.4 atmospheres (ATM) of hypobaric hypoxia 16-19 hours daily for 18 days. Platelet counts first increased with a peak of 1.5 times baseline on day 3 followed by a decline below baseline during the second week of exposure. The greatest effect occurred at 0.3 ATM with a decline of platelets to 15% of baseline as compared to a nadir of 50-80% of baseline at 0.4 ATM. Survival of ^{51}Cr-labeled platelets from untreated donors infused on day 13 of hypoxic exposure was decreased to ½ of control in the 0.3 ATM group but normal in the 0.4 ATM group. Megakaryocyte concentration showed the same trend with a decrease to ½ of control at 0.3 ATM with only a slight decrease at 0.4 ATM. Platelet aggregation with ADP was markedly reduced after two weeks exposure to 0.3 ATM. Aggregation of control platelets suspended in plasma from the 0.3 ATM group was depressed. Aggregation of control platelets resuspended in equal volumes of hypoxic and control plasmas was also decreased. Resuspension of control platelets in control plasma after a 1 hour incubation with hypoxic plasma partially restored the platelet aggregating activity. These studies indicate that exposure of mice to 0.3 ATM of hypobaric hypoxia for two weeks produces thrombocytopenia and decreased platelet aggregation. The decrease in platelet count is associated with decreased platelet survival and megakaryocytes. Decreased platelet survival is associated with an extrinsic rather than an intrinsic platelet defect since normal platelets have a shortened survival in hypoxic mice at 0.3 ATM. The decrease in platelet aggregation is likewise due to a plasma inhibitor since plasma from hypoxic mice inhibits aggregation of normal platelets. The changes in platelet kinetics and aggregation of the mouse exposed to 0.3 ATM for two weeks mimic in many ways those seen in patients with chronic hypoxemia and provide a laboratory model to study these alterations.

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DIFFERENTIAL UPTAKE OF 111-INDIUM BY PLATELETS AND GRANULOCYTES. R.J.Hawker and Carolyn E.Hall. Dept. of Surgery, University of Birmingham, UK.

Mixed cell,leucocyte or platelet preparations labelled with 111-Indium oxine have been used to visualise septic foci, renal rejection and venous and arterial thrombosis. Pure polymorphonuclear leucocyte preparations are difficult to prepare without modification of cellular activity and are generally contaminated with platelets. Up to 27% of the Indium label is associated with platelets when a granulocyte preparation contains as little as 2% of the original platelet population.

Under conditions of limiting Indium-oxine,uptake by platelets is 16.8 and 17.5 times more effective than granulocytes or erythrocytes per unit area of membrane; the accumulation by these latter cell types is related to their surface area with a ratio of 4.7:1. This data is further evidence for a facilitated mechanism for the uptake of Indium by platelets.

Labelled platelets have been used for visualisation of sterile and septic abscesses in animals, and in man minor inflammatory responses can be detected. 99.8% pure platelet preparations are simple to prepare and label. These cells which have a more efficient uptake of Indium and long biological survival (up to 9 days) are capable of detecting a wide range of lesions. The use of labelled granulocytes with a short biological survival (about 4 hours) is restricted to haematological investigations and diagnosis of acute bacterial infections or necrosis.