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COMPARISON OF BLOOD, RED CELL AND WHITE CELL RHEOLOGY IN UNSTABLE ANGINA AND ACUTE MYOCARDIAL INFARCTION. G.D.O. Lowe, G. Thomson, S.E. Lennie, J. Anderson, S.M. Cobbe and C.D. Forbes. University Departments of Medicine and Cardiology, Royal Infirmary, 10 Alexandra Parade, Glasgow, G31 2ER, Scotland, U.K.

In acute coronary artery thrombosis, the flow properties of blood might conceivably influence progression to (a) complete thrombotic occlusion and transmural myocardial infarction, or (b) resolution of ischaemia without infarction (unstable angina). To test this hypothesis, several rheological variables were measured in the following groups of patients, matched for age, sex and smoking habit: (1) acute transmural myocardial infarction (n=15); (2) unstable angina (ischaemic pain and ECG but no significant enzyme rise, (n=16); (3) non-cardiac acute chest pain (n=9); and (4) healthy controls (n=20). Patients with infarction had significantly elevated levels of blood viscosity at high and low shear rates (94 and 0.94 s^{-1}, Contraves LS30) compared to all other groups, associated with significantly higher levels of haematocrit, fibrinogen, plasma viscosity and fibrinogen: white cell count was also significantly higher. These abnormalities could therefore predispose to complete thrombotic occlusion and infarction. Patients with unstable angina also had significant increases in fibrinogen, plasma viscosity and white cell count, intermediate between infarct patients and controls: however blood viscosity increase was prevented by a lower haematocrit, which may predispose to resolution of thrombosis and ischaemia. Red cell deformability (Contraves viscometer and St. George's Filtrometer with 5 μm Nuclepore filters) was normal in infarction and in unstable angina, but significantly decreased in non-cardiac chest pain. Polymorph leucocyte filtration in a positive-pressure system (Nuclepore 5 μm filters) was normal in infarction and unstable angina, and mononuclear leucocyte filtration was only slightly reduced in both groups. Hence the major rheological changes in myocardial infarction and unstable angina are increases in fibrinogen and cell counts, rather than altered cell deformability.

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ULTRASTRUCTURAL INVESTIGATIONS ON THE MECHANISM OF "SHEAR-INDUCED PLATELET ACTIVATION". L.J. Wurzinger (1), R. Opitz (2) and H. Schmid-Schönbein (3). Abt. Anatomie (1), Aerodynamisches Institut (2), Abt. Physiologie (3) der RWTH, Pauwelsstrasse, D-5100 Aachen, F.R.G.

High shear forces are suspected to play a triggering role in the initiation of arterial thrombosis, by activating platelets and the coagulation system. In an earlier study a shear stress of 170 N/m^2 acting for only 7 milliseconds (ms) on platelet rich plasma (PRP) was found to induce a significant increase in platelet factor 3 availability (Thromb. Haemost. 54: 381-386; 1985). To clarify the question whether platelets can be activated directly by mechanical forces in analogy to smooth muscle cells, electron micrographs of platelets subjected to laminar shear stress were analysed with morphometric methods. The level of activation of platelet suspensions was quantified by assessing 1) the elongation of platelet profiles giving a measure for the "flatness" of the discoid resting platelets, and 2) the centralization of granules.
Exposure to a shear stress of 170 N/m^2 for 113 ms leaves ca. 15 % of the platelets irreversibly damaged, featuring degenerative ballooning, with break-down of internal structure and cell membrane defects. The remaining 85 % appear typically activated with rounded shape, extension of pseudopods and centralization of granules. Addition of "ADP-scavengers" to the suspension medium totally changes the appearance of sheared platelets: still a comparable proportion of them has undergone irreversible degenerative changes, but the "surviving" population lacks ultrastructural signs of platelet activation. This is reflected in values of the morphometric parameters which are close to the level of unsheared control samples.
It is therefore concluded that "shear-induced platelet activation" cannot be ascribed to a direct stimulating effect of shear forces, but rather to secondary biochemical activation by adenine nucleotides leaking from a small percentage of shear destroyed platelets. The latter process, however, requires a well stirred though undiluted environment, as it is provided in vortices and eddies.

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HIGH SUSCEPTIBILITY OF RABBIT, DOG, AND PIG PLATELETS TO SHEAR-INDUCED INJURY. J.E. Bauman (1), J.H. Joist (1), G. Vogler (1), and S.P. Sutera (2). Departments of Internal Medicine, Pathology and Comparative Medicine, St. Louis University (1), and Department of Mechanical Engineering, Washington University (2), St. Louis, MO, USA.

In an attempt to develop an animal model for the study of the effects of fluid shear stress on platelet in vivo survival we examined the effects of repetitive short-duration (5 sec) and continuous prolonged (5 min) shear exposure in a cone-plate viscometer and Couette rotational viscometer on platelets (in citrated platelet-rich plasma) from humans, rabbits, dogs, and pigs. Comparable platelet aggregation (PAG = loss of single platelets) (18-64%) was observed with platelets from all species, associated with dense granule release, as a function of shear stress amplitude (25-50 dyn/cm^2) under the conditions used. However, whereas with human platelets, little or no platelet injury (loss of LDH) was observed, appreciable platelet LDH loss was found with platelets from all animal species studied even at the lowest shear stress used, and LDH loss progressively increased with increasing shear stress amplitude (up to 30% at 50 dyn/cm^2), and duration both in the cone-plate and Couette viscometer. These findings indicate a fundamental difference in the response of rabbit, dog, and pig platelets (as compared to that of human platelets) to laminar fluid shear stress in vitro. The mechanism(s) and factors leading to the apparent increased mechanical fragility of the animal platelets as compared to human platelets are currently under investigation.

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THE PRACTICAL VALUE OF THE IN VITRO FILTER BLEEDING TIME. G.P. Salmon and J.R. O'Brien. Central Laboratory, St.Mary's Hospital, Portsmouth PO3 6AG, Hampshire, England.

The in vivo bleeding time has many disadvantages, some of which are obviated by an in vitro filter bleeding time. Normal native or heparinized blood is forced at 40mmHg through a filter made of glass microfibres with tortuous capillary sized pores which retain particles over 10μ. It is found that with high shear platelet aggregation occurs and when about 200,000 platelets (or 70%) of platelets are retained the filter becomes blocked. The test takes about two minutes to perform. Three routine measurements are easily made. (1) The % platelets retained between 10-20 secs; (2) the rate of blocking, e.g. drops 10-20/drops 0-5; (3) the blocking time. The within sample coefficient of variation (c of v) was 9% ± 4, n = 6. The c of v within stable patients studied over six months was 20% ± 11, n = 20. The correlation between platelet retention and the skin bleeding time is good overall when von Willebrand (VW) patients are included (r = -0.73, n = 52) but absent when both tests are within the normal range. This test is sensitive to R:ag values from 0-160 (r = 0.62,n = 52) but poor within the VW and within normal groups. It is also abnormal in some patients with low platelet counts. Atherosclerotics and diabetics have a normal test. Treatment of VW patients with DDAVP or with cryoprecipitate usually normalises this test. In one VW patient neither substance corrected this test and he bled. The test is thus useful in monitoring in vitro and in vivo the efficiency of various factor VIII concentrates to stop bleeding in VW disease. In vitro it is abnormal in the presence of many "membrane-active" drugs. Different drugs also have different effects on the retention of white cells; so it could be useful as a pharmacological screen. Thus it has uses as a quick and easy clinical screen for many forms of platelet-dependent haemostatic defects. It could also be used by the pharmaceutical industry and by producers of factor VIII concentrates.