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 ischemia 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=12); (2) unstable angina (ischemic pain and ECG but no significant enzyme rises, 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 (96% and 0.46 s^-1, Contraves L350) compared to all other groups, associated with significantly higher levels of hemocrit, 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 increases were prevented by a lower hemocrit, which may predispose to resolution of thrombosis and ischemia.

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/m² acting for only 7 milliseconds (ms) could activate platelet rich plasma (PRP) and induce a significant increase in platelet factor 3 availability (Thromb. Haemost. 54: 381-386, 1985). To clarify the question whether platelets could be activated directly by mechanical forces in analogy to smooth muscle cells, electron micrographs of platelets subjected to laminar shear stresses were analyzed 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/m² for 113 ms leaves ca. 15% of the platelets irreversibly damaged, featuring degenerative changes like degranulation, deformations of platelet membranes and cell membrane defects. The remaining 85% appear typically activated with rounded shape, extension of pseudopods and secondary biochemical changes. Inhibition of "ADP-receptors" to the suspension medium totally changes the appearance of "surviving" platelets: still a comparable proportion of them undergoes 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 unhearaed control samples.

It is therefore concluded that "shear-induced platelet activation" cannot be ascribed to a direct, shear-stimulating effect of shear forces, but rather to secondary biochemical activation by adenine nucleotides leaking from a small percentage of shear damaged platelets. The latter process, however, requires a well stirred though undiluted environment, as it is provided in vortices and eddies.

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/cm²) 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 50% at 50 dyn/cm²), 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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