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EFFECTS OF FLOW PULSATILITY ON PLATELET ADHESION TO SUBENDOTHELIUM Hans H.F.I.van Breugel (1), Jan J.Sixma (1), Robert M. Heethaar (2) (1) Dept. of Haematology and (2) Medical Physics University Hospital Utrecht, The Netherlands

Platelet adhesion studies in perfusion chambers are generally performed with constant flow rate or with pulsatile flow generated by a roller pump. No information is available about the effect of flow pulsatility in the physiological range. For this purpose we devised a system consisting of a eccentric rotating disc which forces a driver toward a flexible tube. This movement causes a sinusoidal laminar flow component. The effect of this sinusoidal pulse on platelet adhesion was studied with the annular perfusion chamber of Baumgartner using umbilical arteries and ^{111}In-labeled platelets. Conditions used are described below, where γ_0 [1/s] is the constant flow component, $\bar{\gamma}$ [1/s] is the amplitude of the sinusoidal component and f [beats/min] is the frequency of the pulse (70 beats/min standard). Adhesion values are expressed as 10^5 ^{111}In - platelets/cm^2 (n=4).

(γ_0 = 1800 /s)

$\bar{\gamma}$	Adh	± σ
0	25	± 3
250	32	± 7
500	29	± 7
1000	25	± 6

(γ_0 = 400 /s)

$\bar{\gamma}$	Adh	± σ
0	46	±11
75	45	± 4
150	50	± 6
300	53	± 6

($\frac{\gamma_0}{\bar{\gamma}}$ = 800 /s, = 800 /s)

f	Adh	± σ
0	31	± 4
30	31	± 4
70	30	± 4
120	28	± 2

When oscillatory flow (absence of constant component) was generated, platelet adhesion increased with increasing amplitude of the pulse.

These data indicate that pulsatility as present in the aorta and large arteries has no effect on platelet adhesion.

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PLATELET DEPOSITION ONTO FIBRIN-COATED SURFACES UNDER FLOW CONDITIONS. C. J. Jen and Y.L. Chiu. Department of Physiology, National Cheng Kung University, Medical College, Tainan, Taiwan, Rep. of China.

Fibrin solubilized in NaBr/acetic acid was used to coat glass tubes. Platelet deposition on fibrin-coated surface and release from these adherent platelets were studied in an in vitro flow system. When a mixed suspension of washed platelets and red cells flowed through a fibrin-coated glass tube, only platelets deposited onto the fibrin-coated surface. The density of adhered platelets increased with flow time and decreased with distance from the tube inlet. The adhesion rate increased with increasing shear rates from 45 s^{-1} to 180 s^{-1}. This adhesion process appears to fit a diffusion-limited mathematical model. Comparing with glass and other protein-coated surfaces such as collagen, fibrinogen, or albumin coated surfaces, the number of adhered platelets per unit area decreased in the following order: collagen > fibrin > fibrinogen > glass > albumin. On the other hand, the degree of release reaction from these platelets decreased by another order: collagen > glass > fibrinogen > fibrin. We observed little release from platelets that were in contact with a fibrin-coated surface. Our results support that platelets specifically adhere to fibrin-coated surface and that this interaction does not induce platelet release.

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THE EFFECT OF SHEAR ON OLIGOMER FORMATION; EFFECTIVE REMOVAL OF MONOMERS. H.R. Berk, Duke University, Dept. Biomedical Engineering, Durham, NC, U.S.A.

Fibrin polymerization has been found to be influenced by shear flow conditions (Puryear,1980). In order to determine which mechanisms are responsible for the effect reported it is necessary to look at the various stages in fibrin polymerization. It is known that the enzymatic attack of thrombin on fibrinogen is not influenced by shear (Sellers,1981). The next step, which is investigated in this study, is the oligomer-early protofibril stage.

Fibrinogen (human,Kabi) is reacted with thrombin (human,Sigma) under Couette flow conditions (volume-averaged shear 0-250sec-1) in a pH 6.8, 4mM CaCl2, HEPES buffered solution (I.S.-.15). The reaction time is chosen so that 6% of fibrinopeptide A (FPA) is released. The reaction is stopped by a 1,6 hexandiol-hirudin solution. The effect of shear on oligomer population is measured using large angle lightscattering techniques.

In order to predict theoretical shear effects on oligomer formation, it is important to be able to predict the population size. This is done using Jamney's (1983) predictions, for early reaction time, assuming q=16. Given a size distribution it is possible to apply low Reynold's number hydrodynamic and Smoluchowski's coagulation theories to predict possible shear affects.

Hydrodynamic theory predicts no effect of shear on oligomer formation; Peclet numbers are too small. Smoluchowski coagulation theory, on the other hand, predicts that for oligomer sized particles in the shear range studied, orthokinetic (shear induced) coagulation becomes more important than perikinetic (Brownian) coagulation.

Results obtained from Zimm analysis show a dramatic increase in molecular weight, compared to the stagnant case, in the shear region corresponding to where orthokinetic coagulation dominates. The higher the thrombin concentration, the more extreme and earlier (i.e. lower shear) these effects are felt. After a peak is reached in molecular weight there is a sudden drop. This is caused by monomer exhaustion which shifts the population to a more homogeneous type. The concept of orthokinetic coagulation is important physiologically since it is advantageous to incorporate monomers onto fibers as quickly as possible.

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SYSTEMIC FIBRINOLYSIS AND PLASMA VISCOSITY REDUCTION: A SECOND BENEFIT. A.J. Moriarty, R. Hughes, S.D. Nelson and K. Balnave. Craigavon Area Hospital, Craigavon, N. Ireland.

The aim of this study on a small cohort of patients (N = 30) with acute myocardial infarction (AMI) receiving systemic streptokinase (STK) thrombolytic therapy was to measure the decrease in plasma viscosity concomitant with fibrinogen depletion.

Serial measurements of plasma viscosity, plasma fibrinogen and haematocrit were undertaken in treatment and control groups at times t = 0, 1 hour, 6 hours, 12 hours, 24 hours and daily thereafter over a period of six days. Viscosity was measured at 25°C using a Wells-Brookfield cone/plate digital viscometer, and fibrinogen determination was by the method of Clauss.

Results indicated a mean percentage drop in plasma viscosity of -17% in the STK-treated group with a maximum drop in any one patient in excess of -30%. This contrasted with a mean viscosity rise of almost +20% in the control group with a maximum rise in any one patient of almost +44%, parallelling the rise in plasma fibrinogen as an acute phase reactant.

Correlation studies between viscosity and plasma fibrinogen were strongly positive with mean r-values of 0.74 and 0.66 respectively. Interestingly, mean plasma viscosity in the STK-treated group was still reduced by -5% at 6 days post-therapy.

The conclusions drawn from these data are that the benefit of systemic STK treatment in AMI may in part be due to reduced myocardial workload and oxygen consumption at a critical time through afterload reduction, and improved collateral circulation and microcirculation consequent on the reduced plasma viscosity. Clearly there may be implications for newer tissue-specific agents which do not have a substantial systemic effect.