Time
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0414 PROSTACYCLIN: PRODUCTION BY VASCULAR ENDOTHELIUM AND EFFECTS ON PLATELET AGGREGATION

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The inhibitory effect of vascular endothelial cells on platelet aggregation is due to their ability to release prostacyclin. The existence of an ADPase has been confirmed in endothelial cells but this enzymes does not seem to be related to the anti-aggregating properties of vascular endothelium. In vitro, the release of prostacyclin by humand and rabbit endothelial cells persists after several subcultures. The production of PGI$_2$ can be demonstrated by its inhibition by aspirin-like drugs or 15-hydroperoxy arachidonic acid (a specific inhibitor of PGI$_2$ synthesis). Moreover, the antiaggregating activity is antagonised by an antibody to 5,6 dihydro prostacyclin which cross reacts and neutralises prostacyclin.

0415 PLATELET ADHESION AND AGGREGATION IN ARTERIES OF RATS, RABBITS AND GUINEA PIGS IN-VIVO CORRELATE NEGATIVELY WITH THEIR PROSTACYCLIN (PG I$_2$) PRODUCTION.

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This study investigates whether PG I$_2$ produced locally by the vessel wall is important for the interaction of platelets with subendothelium (SE) in-vivo. Acrtic endothelium in the three species was experimentally removed. Subsequent platelet deposition on SE was assessed by morphometry. After a 10 min exposure, surface-coverage with adherent platelets in rats, rabbits and guinea pigs amounted to 63±4, 82±3 and 97±1% (means ± SE, n>9) with adhesion-induced aggregates to 0±0, 6±2 and 15±4%, respectively. Conversely, as measured by bioassay, excised aortic segments of rats, rabbits and guinea pigs produced 135±14, 34±3 and<<15pmol PG I$_2$/10 mg aorta/30 min incubation in buffer, respectively (n=9). In a second set of experiments, the aorta of an exsanguinated rat was cannulated with Silastic tubing, rinsed with buffer and denuded of endothelium. Blood from the aorta of a heparinized rabbit was then circulated (33±1 ml/min) through the abdominal aorta of the rat and back into the vena cava of the rabbit. Adhesion and aggregation of rabbit platelets on SE of untreated rats after 5 min exposure amounted to 16±7 and 7±4%, respectively (n=8). In contrast, on SE of rats pretreated with aspirin (50 mg/kg p.o.) which inhibits production of PG I$_2$ by >80%, platelet adhesion and aggregation amounted to 43±9 and 24±7, respectively (n=8, 2p <0.05). Conclusion. Platelet adhesion and aggregation on SE in-vivo correlate negatively with the production of PG I$_2$. The data suggest that PG I$_2$-production is an important determinant of blood vessel thrombogenicity.

0416 Fluid Dynamical Considerations of Platelet-Vessel Wall Interaction.

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Platelet adhesion to subendothelium is dependent on two distinct processes: (1) diffusive transport (T) of platelets to the surface and (2) platelet-subendothelial reactivity (R). The relative magnitude of T to R will determine which factors control the adhesion rate. Physical factors, specifically, wall shear rate (γ) and platelet diffusivity (D) influence T, whereas chemical alterations modify R. An increase in the magnitude of γ or D or a decrease in R tends toward R controlled adhesion. An increase in flow rate or decrease in vessel dimensions increases γ, whereas D increases with both red cell concentration (up to 40 %) and γ.

In flowing blood at shear rates comparable to those found in veins or large arteries (< 650 sec^{-1}), T determines platelet adhesion. Moderate alterations in R, such as produced by the addition to blood of 45 mM citrate, 10-100 nM prostacyclin or in Von Willebrand factor depleted blood, have little effect on platelet adhesion values under these flow conditions. However, as shear rate is increased to values comparable to those in the microcirculation (1300-2600 sec^{-1}), the same blood samples show values of platelet adhesion which are reduced compared to controls, and the reduction increases with shear rate. Thus, measurements of R should be determined under controlled shear conditions which are high enough to be outside the range of predominantly transport controlled adhesion.