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0088 PLASMA FROM PATIENTS WITH HEPATIC OR RENAL FAILURE STIMULATES PROSTACYCLIN RELEASE FROM "EXHAUSTED" RAT AORTA SLICES

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Slices of rat aorta (1.5 to 2 mg wet weight) were washed several times in tris buffer until no further release of anti-aggregating activity could be detected. These "exhausted" aorta fragments were then incubated for 60 to 120 min. at room temperature with 250 µl platelet-poor plasma from either a healthy subject or from a patient with hepatic or renal failure. 100 µl of supernatant plasma were subsequently added to 300 µl normal human platelet-rich plasma; the mixture was challenged one minute later with ADP (2 to 4 µM final concentration) and platelet aggregation recorded.

The plasmas from 6/6 uraemic patients undergoing maintenance haemodialysis stimulated prostacyclin release more than the simultaneously studied normal plasmas.

The 17 patients with liver disease were classified using Child's criteria for hepatic functional reserve. Stimulation of prostacyclin release was found with the plasma of 4/4 patients with advanced hepatic dysfunction, 4/6 patients with moderately impaired hepatic function and 4/7 patients with good hepatic function.

Enhanced prostacyclin release may play a role in the pathogenesis of the haemorrhagic diathesis of patients with renal or hepatic failure.

P5-057 0089 BINDING OF PLATELET FACTOR 4 TO CULTURED HUMAN ENDOTHELIAL CELLS

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Platelet factor 4(PF-4) is a product of the platelet release reaction. A well known property of PF-4 is to interact with sulphated glycosaminoglycans(GAGs), including heparin; binding to heparin leads to neutralization of the anticoagulant activity.
This study was undertaken to examine the possible binding of PF-4 to monolayers of cultured human endothelial cells(EC). The EC surface has been shown to expose GAGs, in particular heparan sulphate. Cultures incubated at 37°C with various amounts of ^{125}I-PF-4 bound ^{125}I-radioactivity in a dose-dependent manner. Maximum binding was about 500 ng per 0.7 cm^2 dish(0.4×10^6 cells). About 50% of this was associated with the cells. In the presence of 200 ug/ml of unlabelled PF-4 or 6 ug/ml of heparin the binding was less than 5%. Chondroitin-4-sulphate(30 ug/ml) had little influence on the binding.
The observed EC-PF-4-binding in vitro may reflect a similar interaction in vivo. Such a phenomenon may influence the non-thrombogenic properties of the vascular lining. Furthermore it could affect the reliability of the PF-4 measurements as indicators of intravascular platelet release.

P5-058 0090 HEPARIN - PF_4 PULSING AS A MEASURE OF PLATELET - ENDOTHELIAL CELL REACTION IN VIVO

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iv. Heparin (1000 units) causes an increase in plasma PF_4 of as much as 30-fold, when measured by radioimmunoassay. The PF_4 reaches a peak within 5 minutes after injection and is subsequently cleared to a normal value within 40-80 minutes. The Peak elevation is proportional to the initial heparin dose. Subsequent iv. Heparin doses, within the next few hours, fail to elevate PF_4. Control experiments strongly indicate that the source of the PF_4 is the vascular endothelium rather than the platelets. Further experiments have shown that this PF_4 reservoir half fills within 48 hours. We suggest that iv. heparin pulses can be used for studying, indirectly, platelet - endothelial cell interaction in vivo.