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0302 PROSTACYCLIN CAN REPLACE HEPARIN FOR HAEMODIALYSIS IN DOGS

H.F. Woods*, and M.J. Weston, Renal Unit, King's College Hospital, London.
S. Bunting, S. Moncada, J.R. Vane, Wellcome Research Laboratories, Beckenham, Kent.

Prostacyclin, produced by vascular endothelium, is the most potent inhibitor of platelet aggregation known to man. To assess its effects on platelets during dialysis ten greyhounds were dialysed for 90 minutes with cuprophan coils. At the end of dialysis arterial platelet counts (% of initial value) were significantly higher in the five dogs in which prostacyclin had been infused (115.7 ± 8.6) than in the animals in which heparin alone had been used (77.8 ± 16.8, <0.05). Prostacyclin reduced the extraction of platelets by the dialyser. The screen filtration pressure, a measurement of platelet aggregates in blood leaving the dialyser, remained unelevated in the prostacyclin treated animals (80 ± 11.3 mm Hg) but rose significantly in those infused with heparin alone (249 ± 57 mm Hg, <0.02). In another five dogs infused with prostacyclin but no heparin, dialysis did not reduce platelet count, elevate the screen filtration pressure or alter the overall clotting tests.

Thus prostacyclin enables haemodialysis to be carried out without the undesired effects on platelets and haemostasis that are associated with the use of heparin.

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0303 THE USE OF PROSTACYCLIN (PGI_2) DURING CHARCOAL HAEMOPERFUSION

H.F. Woods* and M.J. Weston, King's College Hospital, London.
S. Bunting, S. Moncada and J.R. Vane, Wellcome Research Laboratories, Beckenham, Kent.

Although charcoal haemoperfusion has been used in the treatment of hepatic and renal failure and of drug and other intoxications, its potential has been limited by thrombocytopenia and other effects on platelet function. To try to improve blood-compatibility of charcoal haemoperfusion we infused PGI_2, the most potent platelet inhibitor known to man, in addition to heparin during charcoal haemoperfusion carried out for 120 minutes in healthy dogs. With PGI_2 platelet counts fell to only 86 ± 2.3% of initial compared to 17 ± 2.7% when heparin alone was used. PGI_2 prevented any rise in screen filtration pressuring during charcoal haemoperfusion (a measure of platelet aggregate formation) whereas with heparin alone the screen filtration pressure quadrupled. During charcoal haemoperfusion with heparin only the plasma fibrinogen levels fell to 54 ± 4% of initial but with heparin plus PGI_2 the plasma fibrinogen levels were maintained at 92 ± 3.8%. Furthermore the use of PGI_2 prolonged the activity of heparin as measured by thrombin clotting time during charcoal haemoperfusion.

This dramatic improvement in biocompatibility during charcoal haemoperfusion when PGI_2 is used may allow more satisfactory assessment of its use for detoxification.

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0304 HEPARIN-COATED SURFACES THAT BIND ANTITHROMBIN HAVE REDUCED PLATELET REACTIVITY

J. Lindon*, D. Brier-Russell, M. Silane, M. Smith, B. Labarre, A. Dincer, R. Rosenberg, E. Merrill, E. Salzman, Depts. Surg. & Med., Beth Israel Hosp., and Sidney Farber Cancer Inst., Harvard Med. School, Boston, and Dept. Chem. Eng., M.I.T., Cambridge, MA., U.S.A.

Surfaces with heparin bound by covalent linkage react with platelets but are passivated by prior exposure to platelet free plasma (PFP), provided they are capable of adsorbing antithrombin III (AT). For example, heparin-agarose beads induce platelet adhesion and aggregation, which are reduced by preincubation of the beads with PFP, but PFP depleted of AT is not effective. The degree of passivation of the beads parallels their removal of AT from PFP. The beads are also passivated by a solution of purified AT.

Furthermore heparin-polymethyl acrylate copolymers made by radical polymerization initiated by Ce^{4+} bind AT, as demonstrated by measurement of AT remaining in solution after adsorption or eluted from the surface after plasma incubation. On such a surface, AT is activated just as by heparin in solution, measured by the ability of heparinized beads to inactivate thrombin (S-2160 chromogenic tripeptide substrate assay) in the presence of AT and by lack of inactivation of thrombin with AT-poor plasma and return of inactivating effect when AT is added back.

Aggregation of platelets by specific heparin fractions in solution appears to be an analogous phenomenon, which is inhibited by antithrombin.