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MONITORING OF HAEMOSTASIS DURING AND AFTER EXPERIMENTAL AUXILIARY LIVERTRANSPLANTATION.

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Haemorrhagic diathesis is a major risk after human orthotopic livertransplantation. Theoretically, auxiliary livertransplantation (APLT) during which a partial livergraft is implanted next to the sick host-liver, should be accompanied with a minor haemorrhagic diathesis. In this study, haemostasis was monitored intensive during experimental APLT. Transplantation was performed in healthy pigs (n=6). There was no subtitution of plasma products or platelet concentrates, nor use of heparin during the operation, thus making it possible to study the effect of the transplantation procedure and the (ischaemic) liver-graft only. Bloodsamples were taken just after induction of anaesthesia, after anastomosis of the Portal Vein, after anastomosis of the Hepatic Artery, 2 and 3 hours post-operative and several days after transplantation (max. follow-up 30 days). A sample was also taken from the first blood outflow from the graft after recirculation. The following parameters were studied: APTT, PT, thrombintime, Normotest(R), fibrinogen, AT-III, plasminogen, α_2-AP, FDP's, platelet-count and haematocrite. Samples taken direct from the first blood outflow from the graft showed a decrease in platelet-count and a prolongation of the APTT, PT and thrombintime, possibly indicating a consumption of platelets and clotting factors in the graft. During operation there was a decrease of α_2-AP, AT-III and platelet-count, while a remarkeble increase was seen during the first week after surgery to concentrations higher than the normal upper limit. At the end of the first week, in four animals an increase in APTT was seen ($\bar{x}$=252%), together with a prolongation of the thrombintime (60 sec.). Because an anti-Xa activity was measurable, an endogenous heparin-like substance might be reponsible for this. None of the animals showed a bleeding tendency during or after transplantation, which indicates that the surgical procedure followed during APLT and the ischaemic graft do not give a serious disturbance of the haemostasis.

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PROTEIN C ACTS AS AN ACUTE PHASE REACTANT IN EQUINE LAMINITIS.

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Equine Colic Syndrome is a disease of horses whose complications include laminatis.This term describes a situation where microvascular damage to the hoof causes degeneration of the interphalangeal laminae,leading to lameness. Vascular studies have suggested that microthrombosis involving the delicate vessels in the hoof,coupled with changes in the platelet count, coagulation factors & elevated FDP's implicate DIC as a potential etiology. Limited test capability in the horse has limited further evaluation of this hypothesis. We have developed an assay for equine protein C activity,our normal range being 70-160% (Mean+/- 2SD). We studied 12 horses with the disease for 5 consecutive days,drawing 1 blood sample per day. Our expectation was that protein C levels would decrease,if DIC was significant,as would be expected in humans. No significant decrease was noted in any horse. However there was a significant increase in the protein C levels beyond the upper limit of the normal range in 10 of the 12 horses by the third day. Five of the 10 horses maintained this elevation beyond the 5th day. Thus protein C changes were more consistent with an acute phase reactant response,rather than reflecting the decrease we anicipated,if the equine DIC parallels human DIC. We are measuring other acute phase reactants to see if equine protein C parallels those. Since our assay is still being evaluated,more data needs to be obtained in this and other equine disease states before any definative role for protein C in equine pathology can be determined. In our laminitis horses,we are devolping assays for antithrombin III and plasminogen which should allow us to evaluate the disease state more completley for any involement of elements of intravascular thrombosis and fibrinolysis in the equine colic syndrome.

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QUANTITATIVE DETERMINATION OF ENDOGENOUS PGI2 RELEASE IN ANAESTHETIZED BEAGLE DOGS.

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A 30/um diameter pore size screen was inserted into an arteriovenous bypass system in anaesthetized, heparin-treated beagle dogs. The arterial blood was directed through the screen by a roller pump at a constant rate. As a result, the pressure proximal to the filter continuously increased (F.Hermán et al.Thromb. Res.44 /1986/,575). The concentration of proximally infused PGI2 that stabilized the filtration pressure curve (pressure stabilizing concentration= PSC) was determined. If it was low enough (between 0.4 and 1.5 nmol/l) we administered the PGI2-releaser bradykinin (1/ug/kg), angiotensin II (0.5/ug/kg) or ADP (20/ug/kg) in bolus dose intravenously. Together with the changes in blood pressure, we observed a transient decrease in filtration pressure. From the pressure changes, based on the previously determined PGI2 concentration-response relationship, we estimated the amounts of released PGI2 as well as the time course of this release. Indomethacin (2 mg/kg i.v.) significantly decreased the PSC for exogenous PGI2 thereby increasing the sensitivity of the method; the release of PGI2 was abolished. The sensitivity of the method could also be increased by infusing BM.13.177 - an endoperoxide, thromboxane receptor antagonist - proximal to the filter (final concentration: 1-10/ug/ml). This substance did not affect the release of PGI2.

We conclude that by using this technique the endogenous release of prostacyclin can be continuously determined provided that PGI2 level exceeds 50 pg/ml.

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A DOG MODEL OF PERIPHERAL ARTERIAL THROMBOSIS: POSSIBLE PHARMACOLOGICAL CONTROL OF VASCULAR OCCLUSION IN A STENOTIZED FEMORAL ARTERY.

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It has been described by several authors that a critical stenosis of a dog coronary artery causes cyclical blood flow variations (CBFV), which are caused by platelet plugging of the vessel. Little information is available on the mechanism of thrombus formation in a stenotized peripheral artery and on the pharmacological control of this phenomenon. Male beagle dogs were anesthetized with sodium pentobarbital, artificially ventilated and prepared for the recording of arterial pressure, heart rate and femoral blood flow. A cylinder of Lexan with internal diameter of 1.6-1.8 mm and a length of 2.0 mm was placed on the femoral artery near the flow probe. This procedure induced CBFV in about 15% of the experiments. If the arterial vessel was previously squeezed with a forcep at the site of stenosis, CBFV were present in 100% of the experiments. Femoral flow at its peak averaged about 30% of control flow and was characterized by a gradual decrease followed by spontaneous abrupt restorations. CBFV were rather constant for at least two hours in dogs without pharmacological treatment thus allowing, by measuring the changes in frequency and severity of CBFV, the evaluation of a drug action on thrombus formation after its intravenous administration. Heparin (50 I.U./kg) was ineffective while ASA (20 mg/kg) reduced or prevented CBFV in about 50% of the experiments. CBFV were always completely prevented by an inhibitor of thromboxane synthetase (UK 38485, 0.5 mg/kg), by chloropromazine (0.5 mg/kg) and by a serotonin antagonist (ketanserin, 0.5 mg/kg). On the other hand, dipyridamole (1.0 mg/kg) and an alpha 1 antagonist (prazosin, 0.1 mg/kg) were not effective. These results are quite similar to those previously reported in the coronary model of CBFV. They suggest some similarity between the process of thrombotic occlusion in different arterial districts and emphasize the importance of thromboxane and serotonin in this particular model of vascular occlusion. Moreover, the striking increase in the percentage of animal showing CBFV after vessel damage is in keeping with the view that vessel wall properties are essential modulators in the process of arterial thrombosis.

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