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PROPERTIES AND VIRUS SAFETY OF A PASTEURIZED ANTITHROMBIN III-CONCENTRATE. H.E. Karges, P. Fuhge and N. Heimburger. Research Laboratories of Behringwerke AG, Marburg, G.F.R.

The possible occurance of up to now unknown human pathogenic viruses makes it necessary to reconsider the strategies for the preparation of each plasma protein concentrate used for substitution therapy. Even up to now safe products may be contaminated by infectious particles in the near future. Hence, each procedure for the preparation of such proteins should critically be checked for the elimination of contaminating proteins and should contain an inactivation step for pathogenic agents.
Since about 4 decades the pasteurization of albumin in presence of stabilizers has been found to be a safe and mild method to inactivate infectious agents. Using the stabilizers glycine and sucrose, we have now been able to pasteurize antithrombin III without the usual changes in molecular properties.
The product is more than 98 % pure and contains only traces of contaminating proteins. The pasteurization does not alter the electrophoretic behavior of the molecule in membrane electrophoresis (ME) and polyacrylamidgel electrophoresis (PAGE). The reactivity with heparin is nearly unchanged as tested by heparin cofactor activity and twodimensional immunoelectrophoresis. No neoantigen formation due to the pasteurization could be detected.

Using model viruses the efficacy of the pasteurization step has been tested. The following results have been obtained: HIV $\geq 10^{6.7}$ (1), CMV $\geq 10^{4.5}$ (2), HSV $\geq 10^{6.8}$ (4), Poliomyelitis virus $\geq 10^{6.9}$ (4); the number in brackets represent the time in hours necessary to totally inactivate the given virus titer.

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FIBRONECTIN CONTENTS AND LEVELS IN BLOOD COMPONENTS DURING STORAGE. N. Müller and U. Velten. Institute of Transfusion Medicine, University of Münster, D 4400 Münster, FRG.

Fibronectin has been proposed to have an antithrombotic effect, protecting against platelet and fibrinogen consumption after injury. For the supply of platelets the possibility of extending platelet storage is important for the management of platelet logistics. This study was designed to determine the effect of storage on the contents and levels of fibronectin (FN) in whole blood and components such as packed RBCs, PRPs and platelet concentrates (PC) in two different plastics. For care of critically ill patients the FN present in components often used in large amounts could supplement the use of purified FN as a source of this opsonic protein. FN protein was assayed using an electroimmunoassay as well as a turbidimetric assay for quantitative determination at 2 day intervals during storage of CPDA-1 stabilized red cells at 4^{0} C for 35 days and daily during end-over-end rotational storage of platelets at 22^{0} C in conventional plastic containers (I) and trimellitate plasticised polyvinylchloride bags (II) (F-763 Biotest). Moreover platelet functional tests, fibrinogen, F XIII and F VIII-complex were tested. FN levels in red cell components gradually decreased during storage until to 40% of the initial levels. Platelets maintained a concentration of 404 ± 70 ug/dl (I) and 378 ± 66 ug/dl (II). There were no significant differences between the values determined in the two different bags over the 8-days storage period. This study demonstrate the stability of FN protein during storage and for more effective use of limited donor resources the FN content of each of these products should be considered when determing the dose of FN for replacement therapy in critically ill patients with FN depletion following trauma and surgery.

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A STUDY ON THE RECOVERY OF FACTOR VIII PROCOAGULANT ACTIVITY FROM RECALCIFIED, HEPARINISED, CITRATED PLASMA. A.M. Cumming, R.T. Wensley, S.E. Cottrell, and I.W. Delamore. Department of Clinical Haematology, Royal Infirmary, Oxford Road, Manchester M13 9WL, U.K.

This study has been carried out to investigate the potential for increasing the recovery of factor VIII procoagulant activity (factor VIII:C), in cryoprecipitates and concentrates, by the use of heparin anticoagulant. Factor VIII:C in citrated plasma has been shown to be stabilised by recalcification and heparinisation of the plasma. Donations of substantially platelet-free and platelet-product-free plasma, anticoagulated by acid citrate dextrose formula A anticoagulant (ACD A), were collected using a combined membrane filtration/centrifugation plasmapheresis device (the HemaSciences "Autopheresis C"(R)). Samples of this plasma were heparinised (over a range from 0.1 to 12.8 iu/ml) and physiological Ca^{2+} levels were restored. Levels of fibrinopeptide A (FpA) of less than 5 ng/ml were measured in all samples (including following the incubation of plasmas at 21°C for 24 hours). This indicated minimal thrombin generation at plasma heparin concentrations as low as 0.1 iu/ml. Fibrinogen degradation fragment Bβ 15-42 levels in these plasmas were comparable to those in ACD A control plasmas and there was no upward trend with increasing heparin concentration. This suggested that heparin-induced formation of plasmin would not adversely affect the stability of factor VIII:C in plasma treated in this way. Cryoprecipitates were prepared in a routine manner from ACD A plasmas collected, by plasmapheresis, into bags containing sufficient heparin and $CaCl_2$ to achieve plasma heparin levels of 0.1 iu/ml and physiological Ca^{2+} concentrations. (As a result of this secondary heparinisation, there was no infusion of heparin into the donors). Analysis of the cryoprecipitates revealed no resolubilisation problems, a significant ($P<0.02$) gain in the yield of factor VIII:C compared with ACD A control cryoprecipitates, and a mean factor VIII:C specific activity of 0.11 iu/mg of total protein (S.D. 0.03, 6 experiments). Pools of plasma collected in the above manner are currently being fractionated to evaluate the resulting factor VIII concentrates.

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THE EFFECT OF EARLY BLOOD TRANSFUSION ON THE OUTCOME OF GASTROINTESTINAL HAEMORRHAGE. SD Blair (1), SB Janvrin (2), CN McCollum (1), RM Greenhalgh (1). Department of Surgery, Charing Cross & Westminster Medical School, London (1) and Crawley Hospital, Sussex (2), UK.

It has been suggested that mortality due to upper gastrointestinal haemorrhage may be reduced by restricting blood transfusion [1]. We have assessed whether this is due to an anticoagulant effect in a prospective randomised trial.

One hundred patients with severe, acute gastrointestinal haemorrhage were randomised to receive either at least 2 units of blood during the first 24 hours of admission, or no blood unless their haemaglobin was less than 8g/dl or they were shocked. Minor bleeds and varices were excluded. As hypercoagulation cannot be measured using conventional coagulation tests, fresh whole blood coagulation was measured by the Biobridge Impedance Clotting Time (ICT). Coagulation was assessed at 24 hour intervals and compared to age matched controls with the results expressed as mean ± sem.

The ICT on admission for the transfusion group (n=50) was 3.2±0.2 mins compared to 10±0.2 mins in controls. This hypercoagulable state was partially reversed to 6.4±0.3 mins at 24 hours ($p<0.001$). The 50 allocated to receive no blood had a similar ICT on admission of 4.4±0.4 mins but the hypercoagulable state was maintained with ICT at 24 hours of 4.3±0.4 mins. Only 2 patients not transfused rebled compared to 15 in the early transfusion group ($p<0.001$). Five patients died, and they were all in the early transfusion group.

These findings show there is a hypercoagulable response to haemorrhage which is partially reversed by blood transfusion leading to rebleeding.

1. Rofe SB, Duggan JM, Smith ER, Thursby CJ. Conservative treatment of gastrointestinal haemorrhage. GUT 1985; 26: 481-4.