ANTITHROMBIN-III AS A DIAGNOSTIC AID IN DISSEMINATED INTRAVASCULAR COAGULATION. R.L. Bick, M.L. Dukes, W.L. Wilson, and L.F. Fekete. Bay Area Hematology, Santa Monica, California, U.S.A.

Antithrombin-III (AT-III)/heparin cofactor is now recognized as a major inhibitor of thrombin and other serine proteases in coagulation. Since the reaction between AT-III and serine proteases is irreversible, AT-III consumption should be expected in pathological intravascular coagulation and attendant generation of thrombin and other serine proteases. Using a new AT-III assay system, unaffected by heparin or fibrinolytic degradation products, AT-III was monitored in 17 patients with DIC. It was found that early and significant decreases occurred in all pts. It was further noted that monitoring of AT-III during therapy for DIC reflected a cessation of AT-III consumption and, thus, appeared to reflect efficacy of therapy in stopping the clotting process. Only 1 of 17 patients failed to show an increase in AT-III with initiation of therapy. In this group of patients, mini-heparin therapy appeared to be as efficacious as large doses of heparin in correcting AT-III consumption and other laboratory abnormalities of acute DIC, and in controlling hemorrhage of acute DIC. Four patients had chronic DIC with malignancy; the use of ASA and dipyridamole corrected AT-III consumption and clinical manifestations in these patients, although the response required more time than with heparin or mini-heparin. These findings suggest that the monitoring of DIC with AT-III levels may be useful in both confirming the diagnosis and, more importantly, in monitoring efficacy of therapy. Significant rises in AT-III were noted in all but 1 patient after initiating therapy, presumably reflecting cessation of consumption. In addition, mini-heparin appeared to be as efficacious as large heparin doses in stopping acute DIC and antiplatelet therapy appeared to stop AT-III consumption and clinical manifestations in patients with chronic DIC associated with malignancy.

INHIBITION OF THE PLATELET RELEASE REACTION IN VIVO BY SULPHINPYRAZONE AND METABOLITES. A.M. White and K.D. Butler. CIBA Laboratories, Horsham, England.

One of the earliest responses in the Arthus reaction to the injection of antigen is a transient thrombocytopenia which reaches a maximum in 15-30 min. This response is apparently associated with the platelet release reaction since it is inhibited by sulphinpyrazone, aspirin, phenylbutazone and indomethacin but not dipyridamole or heparin. It has now been shown that two human metabolites of sulphinpyrazone namely p-hydroxysulphinpyrazone and the sulphone of sulphinpyrazone are equipotent with the parent molecule in inhibiting the thrombocytopenia and by inference the platelet release reaction.

The relative potencies of drugs measured in this way differ markedly from their relative potencies towards collagen aggregation ex vivo. Thus sulphinpyrazone (50 mg/kg) given 1 h before challenge inhibits the thrombocytopenia by 79% but not collagen aggregation ex vivo. Aspirin (10 mg/kg) showed about the same potency in vivo and ex vivo with 47% and 50% inhibition, respectively. Phenylbutazone was less active in vivo than ex vivo. These results again serve to demonstrate the effect of anti-coagulants, particularly citrate, on platelet reactivity towards drugs and emphasize the need for sound in vivo methods.

THE APPLICATION OF THE PYRIMIDOPYRIMIDINE RA 233 FOR PLATELET TRANSFUSION. H.Reuter, H.Borberg and H.Linker. Medizinische Universitätsklinik, Köln, FRG.

As an alternative for the buffy-coat preparation of platelets a combination of the continuous flow centrifugation with the single batch processing technique was examined. The use of the membrane stabilizing agent RA 233 has shown this procedure to be sufficiently useful for clinical application. The use of RA 233 made available platelet yields of about 10^{12} platelets per blood donor. The drug was given in an amount of 100 mg i.v. to the blood donor and added in doses of 80 mg to each 500 ml plasma collection bag containing 10% ACD-A solution as an anticoagulant. From the platelet rich plasma the platelets were obtained by further concentration in a Christ IV KS blood bank centrifuge with 2.600 x g. As could be shown by transfusion of RA 233 prepared platelets to leukemic patients the drug is reversibly bound to the platelet membrane. While during preparation platelet adhesion and aggregation are slightly inhibited by RA 233, the functional activity of the platelets is regained after transfusion. The survival of transfused ^{51}Cr -labeled platelets prepared in the presence of RA 233 was found to be in the normal range.