

THE FACTOR VIII RESPONSE TO HIGH PURITY PORCINE FACTOR VIII CONCENTRATE IN ACQUIRED VON WILLEBRAND'S DISEASE. F.E. Preston and R.G. Malia. The University Department of Haematology, Royal Hallamshire Hospital, Sheffield, U.K.

Two patients with acquired von Willebrand's disease were given an infusion of 2000 units of high purity porcine factor VIII (Hyate) which we previously have shown contains only negligible amounts of FVIII:Ag. The disappearance of half life of FVIII:C was 2 hours and 3½ hours. In one patient a marked secondary rise in FVIII:C occurred 1 hour after completion of the infusion. In both patients ristocetin-induced platelet aggregation rose from zero to 10 per cent and 70 per cent respectively between the first and second hour with accompanying rise in human FVIII:Ag measured by specific non-crossreacting immunoradiometric assays. These observations suggest that porcine FVIII:C induced de novo synthesis or release of human FVIII:Ag. However an alternative explanation would be dissociation of a FVIII:Ag-antibody complex since we have demonstrated antibody directed against the Factor VIII complex in these and other patients with acquired von Willebrand's disease.

A POSSIBLE ROLE OF FACTOR VIII COAGULATION AND CYCLIC NUCLEOTIDES IN PROMOTING ENDOTHELIAL RENAL INJURY. E. Bertaglia, U. Vertolli, V. Pengo, B. Baggio, C. Tessarin, P. Belmonte, R. Zanella. Clinica Medica I University of Padua, Padua, Italy.

To evaluate a possible interaction between coagulation factors, inflammation, and immunological disorders in the pathogenesis of glomerulonephritis (G.N.) factor VIII clotting activity (VIII:C), related-antigen (VIII:Ag), urinary fibrinogen degradation products (F.D.P.) excretion and cyclic nucleotides (cAMP) in 21 patients affected by chronic G.N. with normal renal function, was investigated. These patients were followed-up for two years. For the assay of factor VIII:C, a factor VIII deficient plasma was used. Factor VIII:Ag were assayed by rocket electroimmunodiffusion in agarose gel, urinary F.D.P. by Thrombo-Wellcotest and cAMP by radioimmunoassay. The same tests were performed in 25 healthy controls. Patients' clotting activity, measured at first admission, showed a significant decrease in comparison with the values obtained at the end of the follow-up period ($t=-2.61$ $p<0.02$). The clotting activity of the renal patients was lower than in controls ($t=2.09$ $p<0.05$). However, factor VIII:Ag was significantly increased in the same patients. A significant direct correlation between the urinary excretion of cAMP and plasma concentration of factor VIII:Ag ($r=0.82$ $p<0.001$) as well as between urinary F.D.P. and cAMP excretion ($r=0.49$ $p<0.05$) was found, when the patients were classified according to the morphological findings of the kidney biopsy. Most probably a circulating thrombin excess leads to consumption of factor VIII:C and promotes the extrusion of cyclic nucleotides from intracellular sites. The relationship found between factor VIII:Ag, cAMP and F.D.P. besides showing a linkage between inflammation and coagulation, seems also to suggest a role for both factors in promoting a renal injury.

FACTOR VIII ANTIGEN AND VENOSTASIS TEST IN DIABETES MELLITUS. A POSSIBLE USEFUL TOOL TO DETECT A LATENT ENDOTHELIAL SUFFERING. R. Giustolisi, R. Musso, T. Lombardo, M. Russo and E. Cacciola. Chair of Haematology, University of Catania, ITALY.

In the mature onset Diabetes Mellitus (DM) high levels of Factor VIII antigen (FVIII R:AG) were reported (Bensoussan et al., 1975, Diabetologia 11, 307; Lufkin et al., 1979, Metabolism 28, 63). The elevated FVIII R:AG levels observed in DM, as well as in other vascular diseases, were claimed as an index of endothelium damage (Boneu et al., 1975, Lancet 1, 1430; Corda et al., 1979, Thrombos. Res. 14, 805). Moreover, since the FVIII R:AG is involved in platelet adhesion to sub-endothelium, its increase might have prognostic significance as thrombogenic risk factor. But, in DM plasma FVIII R:AG levels could be also within normal range, so that the significance as index of endothelial suffering in such evenience would be lacked. Here we report evidence that in DM without clinical signs of vasculopathy, even if the FVIII R:AG plasma levels are in the normal range, the existence of endothelial suffering could be likewise detectable by the simple venostasis test, which, notoriously, represents a damaging endothelium stimulus. To test such a possibility we investigated the behaviour of plasma FVIII R:AG levels after venostasis (performed at forearm pressure of 10 mmHg over diastolic x 20 min) in 12 diabetic patients without overt signs of vasculopathy and exhibiting FVIII R:AG in normal range. This group was matched with 10 normal subjects of comparable sex and age. Measurements of the serum LDH levels before and after venostasis served to prove cellular damage when they increased more than 50%. The diabetic patients showed after venostasis an increase of FVIII R:AG (Laurell's method) which was significantly higher than normal controls ($P<0.005$). Therefore it might be assumed that in diabetic subjects a latent vascular endothelium suffering, even without overt signs of vasculopathy, could exist and it could be detectable by venostasis test.

RELATIONSHIP BETWEEN FACTOR VIII:Ag, FACTOR VIII C AND GLYCOEMIC CONTROL AND VASCULAR COMPLICATIONS IN INSULIN-DEPENDENT DIABETICS. V. Tantalò, E. Rossi, M. M. Cossu, *P. Migliavaccà, *V. Saibene

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Increased levels of Factor VIII are usually reported in diabetes mellitus, even if contradictory relationships with the vascular complications have been observed, due to unselection of patients. We have measured Factor VIII:Ag and Factor VIII C (two stages method) in 60 insulin dependent diabetics (IDD), aged between 7 and 78, compared to 25 sex and age matched normal controls (NC). The presence of retinopathy (r) or macroangiopathy (m) was assessed by fluoroangiography and EKG plus oscillography, respectively. Results are in the table:

	NC	IDD-r-m	IDD-r-m	IDD-r+m	IDD all
FVIII:Ag	106±7	93±6	124±18	135±11	113±6
mean±SEM		n.s.	n.s.	$p<0.025$	n.s.
FVIII C	94±5	126±9	166±18	221±23	165±10
		$p<0.025$	$p<0.001$	$p<0.001$	$p<0.005$

No significant correlations were found between FVIII:Ag, FVIII C and concomitant blood glucose, glycosylated hemoglobin, GH, and the duration of diabetes. A progressive increase in FVIII:Ag according to the extent of the vascular damage is evident. An enhancement of the level of FVIII C, greater than that of FVIII:Ag, index of enhanced thrombin production, is already present even in absence of vascular damage in IDD, being more pronounced in patients with vascular complications.