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INVESTIGATIONS ON MULTIMERIC STRUCTURE OF PLATELET VON WILLEBRAND FACTOR IN PATIENTS WITH HEREDITARY DISORDERS OF PLATELET FUNCTION. Zs. Vigh, I. Scharrer. Department of Internal Medicine, University Hospital, Frankfurt, West Germany

Von Willebrand factor (vWF), a multimeric glycoprotein, plays an essential and multifunctional role in the hemostatic process. It is well known that platelet glycoproteins IB, IIB and IIIA contain receptors for vWF. Von Willebrand factor was also found in alpha granules of platelets. Therefore we investigated the multimeric structure of platelet vWF in 12 patients with different inherited disorders of platelet function. The patients had the following diagnosis: Hermansky Pudlak syndrome, Thrombasthenia and up to now undefined hereditary disorders of platelet function. The method is based upon:
1) washing of platelets 2) release of platelet vWF 3) separation of vWF multimers by SDS-agarose electrophoresis 4) subsequent blotting of vWF multimers onto nitrocellulose 5) staining by peroxidase conjugated antibodies.
The investigations were repeated 3 times and compared to those of normal platelets. In 2 patients with Hermansky-Pudlak syndrome no multimeric structure could be detected in platelets whereas the multimeric pattern of plasma of these patients was normal. Also in one patient with the tentative diagnosis: thrombasthenia we couldn't find any multimeric structure in platelets compared to the normal multimeric composition of plasma.In 2 patients with giant platelets the multimeric distribution was normal. In the remaining 6 patients we observed multimeric structure which was different from that seen in vWd variants and in healthy volunteers. In 1 patient we found normal multimeric pattern in plasma and platelets.
Based on our findings it can be assumed that the analysis of multimeric structure of platelet vWF can be helpful for the diagnostic approach and for the insight in pathogenesis of inherited disorders of platelet function.

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VASCULAR DAMAGE AND FACTOR VIII RELATED ANTIGEN IN THE RHEUMATIC DISEASES. J.J.F. Belch, A. Zoma, I.M. Richards, K. McLaughlin, R.D Sturrock, C.D Forbes. The University Department of Medicine, Royal Infirmary, Glasgow, Scotland, U.K.

F.VIII is produced by the blood vessel wall. Noxious stimuli increase endothelial release of F.VIII Related Antigen (VIII R:Ag). It might be expected that the development of vasculitis would be associated with increased levels of VIII R:Ag. Eight patient groups have been studied; 25 patients with systemic sclerosis, 19 with systemic lupus erythematosus, 15 with rheumatoid arthritis (RA) plus vasculitis, 19 with systemic vasculitis and 14 with atherosclerosis. These were compared to 29 patients with primary Raynaud's Disease, 15 with RA without vasculitis and 50 controls. Results show that where there was evidence of vascular disease, VIII R:Ag was elevated.

Patient Group (median [range])	VIII R:Ag
1. Systemic sclerosis	200 (76-390)*
2. Systemic Lupus Erythematosus	180 (100-370)*
3. Rheumatoid Arthritis plus Vasculitis	300 (160-500)*
4. Systemic Vasculitis	235 (160-430)*
5. Atherosclerosis	188 (140-348)*
6. Primary Raynaud's Disease	140 (71-230)*
7. Rheumatoid Arthritis without Vasculitis	100 (68-190)
8. All Controls	100 (38-195)

* p <0.01 (Mann Whitney)

VIII R:Ag appeared a more specific marker for vascular damage than ESR or CRP. Further longitudinal studies in 11 patients showed good correlation between progression of vascular disease and VIII R:Ag.

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ABNORMAL STRUCTURE OF VON WILLEBRAND FACTOR IN MYELOPROLIFERATIVE SYNDROME IS ASSOCIATED WITH EITHER THROMBOTIC OR BLEEDING DIATHESIS: M.F. López-Fernández (1), C.López-Berges (1), R. Martín (1), A. Pardo (2), F.J. Ramos (1) and J.Batlle (1). Dept. Hematology, Hospital Clínico, Universidad de Salamanca, Spain (1) and Dept. Hematology, Hospital Ramón y Cajal, Madrid (2).

The multimeric and subunit patterns of plasma von Willebrand factor (vWF) were analyzed in eight patients with myeloproliferative syndrome (MS) in order to investigate the possible existence of heterogeneity in the "in vivo" proteolytic cleavage of the protein, previously observed in this entity. Six patients lacked large vWF multimers, five of them having normal bleeding times (BT) and clinically documented episodes of thrombotic origin, whereas one patient had long BT and bleeding symptoms. Seven patients showed an increase 176 kDa subunit fragment while the 189 kDa polypeptide was increased in only one. In addition, another patient (and prior to any therapy) showed the presence of a new fragment of aproximately 95 kDa which disappeared after Busulfan therapy. The collection of blood from these patients with proteinase inhibitors did not correct the abnormalities.
The infusion of DDAVP to two patients with abnormal vWF was accompanied by: the appearence of larger vWF multimers which disappeared rapidly from plasma; an increase in the relative proportion of the satellite bands of each multimer and a further increase in the 176 kDa fragment. These data show some heterogeneity in the vWF abnormality present in MS which may be related in part to a variable degree of proteolysis of vWF ocurring "in vivo" rather than "in vitro", and which may be associated to either a bleeding or (even) a thrombotic diathesis. They also suggest that despite the presence of abnormal, already proteolyzed vWF, DDAVP-enhanced proteolysis occurs in MS to a similar extent as described in normal individuals.

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STUDIES ON THE MULTIMERIC COMPOSITION OF VON WILLEBRAND FACTOR IN CHRONIC MYELOCYTIC LEUKEMIA. W. Tatewaki, H. Takahashi, M. Hanano, S. Takizawa, A. Hattori and A. Shibata. The First Department of Internal Medicine, Niigata University School of Medicine, Niigata, Japan.

In chronic myeloproliferative disorders, thrombohemorrhagic complications occur occasionally in association with high platelet count. These patients may have acquired platelet dysfunction, but no apparent relationship with clinical symptoms has been found. Recently, the abnormalities of the multimeric composition of von Willebrand factor (vWf) have been shown in some patients with essential thrombocythemia and polycythemia vera. We studied the multimeric composition of vWf in 31 patients with chronic myelocytic leukemia (CML); 20 in chronic phase (CP) and 11 in blast crisis (BC). vWf multimer was analyzed by SDS-1.2% HGT agarose gel electrophoresis, followed by visualization with an immunoperoxidase staining. Small (multimer band 1-5), medium (band 6-10) and large (band ≥11) multimers were calculated by densitometer scan. Relative amount of large multimers was 15.5±1.6% (mean±SD) in normal controls, 10.1±5.3% in CP and 15.0±5.5% in BC. CML patients in CP (but not in BC) had smaller amount of large multimers than normal controls ($p<0.001$). Marked decrease in large multimers (<5% of total vWf) was observed in 5 patients (25%) in CP and one patient (9%) in BC. The amount of large multimers was positively correlated with ristocetin cofactor/vWf:Ag ratio ($p<0.01$) and granulocyte counts ($p<0.05$), and was negatively correlated with platelet counts ($p<0.001$). We conclude that some patients with CML, especially in CP, lack large multimers. The negative correlation between the amount of large multimers and platelet counts suggests that large multimers are consumed in high platelet count states.