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HYPERACTIVITY OF PLATELETS TO 5-HYDROXYTRYPTAMINE IN PATIENTS WITH CARDIOVASCULAR DISEASES. J. De Crée, V. Roels and H. Verhaegen. Clinical Research Unit St. Bartholomeus, Jan Palfijn Hospital B-2060 Merksem, Belgium.

Controversy still exists about the exact role of platelets in the pathogenesis of atherosclerosis. However, patients with cardiovascular (CV) diseases have been reported to have enhanced platelet activity and to show hyperaggregability in response to common aggregators. Very little is known on 5-hydroxytryptamine (5-HT)-induced platelet aggregation in these patients. In a previous preliminary study we observed an increased sensitivity of platelets in response to 5-HT in patients with CV diseases. We further showed that ketanserin, a selective 5-HT receptor antagonist both on platelets and vascular tissue, abolished the 5-HT dependent hyperreactivity of platelets in patients with CV diseases. In a prospective study we investigated platelet aggregation in response to 5-HT at 2 x 10^{-5}Mol in 405 patients with various CV diseases as compared with an age-matched control group of 110 apparently healthy donors. Evaluation of the results was based on the presence of a second irreversible aggregation in response to 5-HT. The control subjects responded to 5-HT with a shape change and a weak, reversible aggregation, except for 9 of the 110 volunteers, where a second irreversible wave occurred (8%). In contrast, it was found that 119 out of 405 patients with CV diseases had a biphasic irreversible aggregation (29%) (Chi-square test : $p < 0.0001$). From these 405 patients 129 patients suffered from an acute myocardial infarction (AMI), between 4 and 14 days after the onset of symptoms, 78 patients suffered from ischemic heart disease (IHD), 99 patients from peripheral arterial obstructive disease (PAOD) and 99 patients from diabetes, without clinical symptoms of atherosclerosis. A secondary irreversible platelet aggregation to 5-HT was observed in 36% of patients with AMI, in 22% of patients with IHD, in 25% of patients with PAOD and in 31% of patients with diabetes, all the subgroups being significantly different from the control subjects ($p < 0.01$). These findings suggest that platelets may play a role in the propagation and manifestations of CV diseases and that in diabetes the enhanced platelet activity may be a contributing risk factor in de development of atherosclerosis. Finally, since 5-HT is a potent mediator of vasospasm, treatment with ketanserin might be of therapeutic value in atherosclerosis, where platelet activation is thought to be involved.

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SERENDIPITOUS PROTECTION FROM PLATELET-MEDIATED DISORDERS IN STEROID-TREATED PATIENTS? H. Holloway, A.J. Moriarty, S.D. Nelson and K. Balnave.
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The aim of this study is to investigate the influence of exogenous corticosteroids on platelet aggregation. This is widely recognised to be of significance in the pathogenesis of acute myocardial infarction and other vascular/haematological disorders.

Blood was taken from a cohort of patients (N = 10) undergoing treatment with ACTH or corticosteroids for varied systemic illness. Ex vivo measurements of platelet parameters were made with a Coulter Counter Model S Plus III on non-anticoagulated blood directly from the circulation. Subsequently, aliquots of anticoagulated blood in batches of five were processed at intervals over 24 hours. For comparison, a similar study was undertaken in normal volunteers not on any medication. The mean percentage changes ± standard deviations over the 24 hour interval in platelet count (PLT), mean platelet volume (MPV) and plateletcrit or biomass (PCT) in the respective groups were as follows:-

PLT: $-(3.12 \pm 2.68)$ vs $-(14.77 \pm 3.96)$ ($p < 0.001$);
MPV: 28.88 ± 8.92 vs 46.68 ± 12.54 ($p < 0.01$);
PCT: 25.18 ± 8.16 vs 23.75 ± 8.97 (NS).

The in vitro alteration in PCT over 24 hours in both cohorts is similar and is due to platelet swelling. The change in MPV is partly due to swelling and partly due to aggregation as evidenced by the decrease in PLT. The significantly smaller drop in PLT and smaller rise in MPV in the steroid-treated group clearly demonstrate that platelets from these patients are less aggregable. A possible cause is that the inhibitory effect of steroids on phospholipase may lead to reduced levels of thromboxane A_2. Thus patients on steroid therapy or with high endogenous steroid levels may enjoy serendipitous protection from a variety of platelet mediated disorders. The work may also explain in part why such patients are more prone to bleeding diatheses.

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PLATELET FUNCTION AND LIPOPROTEINS IN PATIENTS WITH HYPOTHYROIDISM.
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Platelet function and serum lipoprotein levels were studied in ten patients (two males and eight females) with hypothyroidism. Platelet aggregation and ATP release were determined by Lumi-aggregometer using ADP, collagen and epinephrine as stimulants. Platelet factor 4 (PF4) and thromboxane B_2 (TXB2) were determined by radioimmunoassay. High density lipoprotein-cholesterol (HDL-C) was determined by heparin-manganese method. HDL subfractions were separated by gradient gel electrophoresis (PAA 4/30). Apolipoproteins were measured by single radial immunodiffusion.

Platelet aggregation increased in those patients at stimulating by epinephrine. ATP release also increased at stimulating by epinephrine. PF4 increased at stimulating by epinephrine. TXB2 increased at stimulating by ADP or epinephrine significantly ($p < 0.05$), respectively. Platelet aggregation was not correlated with thyroid hormones or total cholesterol levels. But it had a positive correlation tendency with HDL-C or HDL_2-C and a negative one with HDL_3-C levels.

These results suggested some relationships between platelet function and HDL metabolism in patients with hypothyroidism.

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CHILDHOOD HEMOLYTIC UREMIC SYNDROME (HUS) : VON WILLEBRAND FACTOR (vWF) AND PLATELET AGGREGATING ACTIVITY (PAA) STUDIES. **SCHLEGEL N. ****MOAKE J., **LGIRAT C., *HURTAUD MF., ***LEVY-TOLEDANO S., **MATHIEU H.-*Lab. Cent. Hemato. and **Clin. Ped.,HÔp.BRETONNEAU, ***INSERM U150, PARIS-FRANCE; ****Methodist Hosp., HOUSTON-U.S.A.*

It has been suggested that a vWF High Molecular Weight Multimers (HMWM) decrease or a PAA were involved in the pathogenesis of HUS. We have studied 8 children (6 girls, 2 boys; 7 months-8 1/2 years old) with HUS : plasma creatinine (µmol/l; mean(range)=306 (105-524), hemoglobin (g/100ml)=7(6.3-7.8), schistocytes (%)=8(1-18), platelets ($x10^3/mm^3$)=57(10-115). The vWF was studied quantitatively (antigen : vWF RAg assay) and qualitatively (multimeric pattern : immunoblotting and autoradiography). PAA studied by incubating the patient's platelet poor plasma (PPP) with washed normal platelets (aggregometer, % light transmission) and confirmed by Thromboxane B_2 (TXB_2) assay and $[^{14}C]$ Serotonine release study. The PAA was characterized by studying the in vitro effect of several platelet aggregation inhibitors, Immunoglobulins (Igs) and Fresh Frozen Plasma (FFP) on the platelet aggregation.

An increase of vWF RAg (%) was observed in 6 cases : mean:330, and possibly related with renal failure. A vWF HMWM decrease was found in 3 patients : 2/3 with associated infection(E.Coli, Pneumococcus), 1/3 with severe hemolysis. Two of these 3 patients had a favourable renal outcome and 1 a severe course (chronic hemodialysis, Arterial Thrombotic MicroAngiopathy at renal histology).An important PAA was evidenced only in 1 patient : post bone-marrow graft HUS during neuroblastoma(NB),arterial hypertension and chronic renal failure. This PAA was Ca^{++}, TXB_2 and cAMP dependent; it was moderately inhibited in vitro by Igs and FFP, but persisted after 5 days of Igs infusion (0.3g/Kg/day). Treatment with aspirin and dipyridamole (10mg/Kg/day each) suppressed the patient platelet auto-aggregation although the PAA persisted (follow up:10months). The PAA did not seem to be related with the NB (absence of GD_2 ganglioside, specific marker of NB); it could be related with anti platelet antibodies. The coexistence of the two abnormalities could not be demonstrated in our patients.

In conclusion, a vWF HMWM decrease was found in 3 out of 8 children patients with HUS. Its presence was not correlated with the severity of the disease. We could demonstrate the presence of PAA during childhood HUS in only 1 post bone-marrow graft case. The PAA characterization is useful for therapeutic decisions and contributes to a better pathogenetic understanding.

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