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THE PROFILE OF IN VIVO PLATELET ACTIVATION IN NOCTURNAL ASTHMA. J.E.J. Morrison (1), A.B. Latif (2), C. Mason (3), P. Bramley (1) & T.R. Craig (1). Pulmonary Research Laboratory (1) and Cardiac Research Laboratory (2), Killingbeck Hospital, Leeds, UK and School of Biomedical Sciences, Bradford University, Bradford, UK (3).

The precise pathophysiology of nocturnal asthma still remains to be elucidated. Activated platelets have the ability to release potent broncho- and vaso-constrictors and therefore, have been implicated in asthma. However, there is no information on the status of in vivo platelet activation in patients with nocturnal asthma.
In a randomised controlled study five healthy volunteers and five asthmatics were investigated during a period of 24h after acclimatisation for one day. Both peak flow rate (PFR) and blood samples were obtained at 4 hourly intervals. Plasma levels of platelet factor 4 (PF4) and beta- thromboglobulin (BTG) were measured by radioimmunoassay and adrenaline (A), noradrenaline (NA) and dopamine (DOP) by radioenzymatic analysis.
PFR (l/min) for the 24h period was significantly lower in asthmatics (401±15SEM, P<0.001) than in controls (598±4SEM) with an apparent circadian rhythm peak (442±73, P<0.05 Wilcoxon's test) at 4.00pm only in asthmatics. Although there was no significant differences in either PF4 and BTG (ng/ml) or A, NA and DOP (nmol/l) between asthmatics and controls an apparent circadian rhythm in all of these parameters was demonstrated in both groups. Peak values (mean+SEM) for PF4 (8.9±1.5) and BTG (44.4±3.8) occurred at 8.00am whereas the highest values for the catecholamines (A: 0.36±0.08, NA: 1.75±0.23, DOP: 0.78±0.16) were observed at 4.00pm indicating a lag of 8h between the peaks for catecholamines and the platelet specific proteins.

These initial data demonstrate a clear difference in PFR between asthmatics and controls which is apparently not associated with changes in either PF4 or BTG but which may concur with circadian changes in plasma levels of catecholamines at least in asthmatic patients. Thus, in vivo platelet activation is probably not a contributing factor in nocturnal asthma. Finally, the phase lag between peak plasma levels of platelet proteins and catecholamines requires further investigation.

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PLATELET RELEASE DURING EXERCISE IN PACEMAKER PATIENTS. Y. Myreng, K. Giesdal, S.E. Kjeldsen, K. Lande, I. Eide and H. Grendahl. Department of Internal Medicine, Oslo University Hospital Ullevål, 0407 Oslo 4, Norway.

Seven pacemaker patients with complete AV-block were studied during one to three week periods of either ventricular (VVI), or atrio-ventricular pacing (DDD) or triggered ventricular pacing (VAT). At rest, the plasma β-thromboglobulin (BTG), arterial adrenaline and nor-adrenaline as well as atrial rate were not significantly different during standard and physiological pacing. Following ergometer bicycling, BTG increased significantly ($p < 0.004$), and more so in VVI pacing (from 38 ±15 to 73 ±15 ng/ml) compared to DDD (27 ±6 to 44 ±13), $p<0.05$. Arterial plasma adrenaline at baseline was 60 ±27 in VVI and 58 ± 27 pg/ml in DDD, with increases during exercise to 353 ±197 and 338 ±164 respectively. Neither was any noradrenaline conc significantly different: 253 ±74 to 2962 ±2031 in VVI versus 226 ±143 to 2848 ±2032 during DDD at rest and during exercise, respectively. The atrial rate was 73 ±11 at baseline increasing to 125 ±15 ppm, versus 69 ±12 to 127 ±15 ppm (ns).
Physiological pacing is thus associated with lower platelet release at baseline (ns, $p<0.07$) and exercise ($p<0.05$), despite no significant difference in arterial catecholamine concentration or the related atrial rate. Increased blood turbulence during atrio-ventricular asynchrony may contribute to the increased release in VVI-pacing.

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ASPIRIN EFFECT ON PLATELET ANTIPLASMINS RELEASE. A.I. Woods, M.A.Lazzari. Department of Haemostasis and Thrombosis, Instituto de Investigaciones Hematológicas "Mariano R Castex", Academia Nacional de Medicina. Buenos Aires Argentina.

It was shown platelet antiplasmin activity which is released by collagen(Col)and thrombin, probably associated with a-granules. Lysis area produced by euglobulins(eug) of PPP and PRP whether or not previously treated with ADP(5uM), Col(20ug/ml) and aspirin(ASA)(80ug/ml)in plasminogen- free-fibrin plates were studied. Results(mm^2) were: eugPPP: 151.3±39.8; +ADP: 155.7±47; +Col: 155.5±50.8; +ASA: 160±42. - EugPRP: 142±42; +ADP: 145±72; +Col: 136±43; +ASA: 138±47. - EugPRP produced slightly lower lysis area than eugPPP(p:ns). ADP, Col and ASA neither modify the lysis area of eugPPP nor of eugPRP. Washed platelets(WP)whether or not treated with ASA were resuspended in eugPPP and then treated with Col(2 and 20ug/ml). Results(mm^2)were: eugPPP: 109.8*35; +3x10^5WP/ul: 66.4±24; +10^6WP/ul: 63±17; +2x10^6WP/ul: 58.4±13. - With Col(20ug/ml): eugPPP: 101.3±28; +3x10^5WP/ul: 48.4±14; +10^6WP/ul: 46.2±16; +2x10^6WP/ul: 44.5±12; +2x10^6WP/ul+ASA: 45.2±8. - With Col(2ug/ml): eugPPP: 103±25; +2x10^6WP/ul: 49±10; +2x10^6WP/ul+ASA: 50.9±13. WP in eug PPPshowed lower lysis area than eugPPP($p<0.001$). The higher number of platelets, the lower lysis area. Col-treated WP showed greater inhibition of lysis area than non-treated WP. ASA could not inhibit this effect.
Conclusion: In eugPRP there was a slight antiplasmin activity related with platelets not completely eliminated from eug fractionation. WP in eugPPP showed higher antiplasmin activity. High and low doses of Col produced antiplasmin release. ASA could not inhibit its release with both doses of Col. We must consider the possibility that platelet antiplasmins could be released by different metabolic pathways other than cyclooxygenase way or they are not stored in the a-granules.

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HEPARIN-RELEASED PLATELET FACTOR 4 (HR-PF4) IN DIABETIC MICROVASCULAR DISEASE. C. Boschetti (1), A. Vicari (2), E. Cofrancesco (1), M. Cortellaro (1), A. Della Volpe (1), G. Moreo (1), E. Pogliani (1), G. Pozza (2), E. Polli (1). Istituto di Scienze Mediche, Università di Milano (1) and Istituto Scientifico S.Raffaele Milano (2), Italy.

When heparin is injected i.v. as a bolus, PF4 but not β-thromboglobulin (βTG) is released immediately. HR-PF4 is not liberated from platelets but from the endothelial cells of vessels which serve as storage sites. The role of platelet activation in diabetic microvascular disease is still controversial, however there is experimental evidence of vascular injury and hemostatic activation preceding the appearance of microvascular disease. The contradictory results so far obtained in man may be partly attributed to the heterogeneity of the diabetic patients studied. We studied 20 insulin-dependent diabetics (age 21-40) in stable metabolic equilibrium (mean HbA_{1c}=7.6%). 10 without fluoroangiographic evidence of retinopathy (Group 1) and 10 with retinopathy (Group 2). None had signs or symptoms of macrovascular disease. The control group consisted of 10 healthy volunteers (age 22-39). No medication except insulin was taken for at least 10 days preceding the study. 12 h before the study all subjects received aspirin 500 mg p.o. Plasma βTG and PF4 were determined before (basal) and 5,30,90 min after a heparin bolus i.v. (5000 U). Protein C, factor VIIIR:Ag and tissue plasminogen activator were also measured in plasma. Plasma βTG and PF4 are listed as mean and SD in the table:

	PF4 ng/ml				βTG ng/ml			
	basal	5 min	30 min	90 min	basal	5 min	30 min	90 min
Controls	3.39	201.00	41.10	9.57	23.50	32.30	28.40	25.45
	2.43	81.71	13.54	5.12	11.08	18.37	12.71	11.98
Group 1	3.47	283.00	36.10	6.50	24.40	26.40	27.70	23.40
	2.86	79.20	12.31	4.57	8.99	11.96	13.12	9.13
Group 2	3.86	210.63	42.50	12.86	39.86	38.25	33.63	43.38
	2.48	150.63	28.22	14.45	18.16	21.06	19.60	25.76