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PLATELET FUNCTION IN VASOSPASTIC DISORDERS. D. Wilkinson (1), P. Vowden (1), L. Gilks (2), S.M. Rajah (2), and R.C. Kester (1). Departments of Vascular Surgery (1) and Haematology (2), Seacroft Hospital, Leeds, U.K.

If vasospastic disorders are associated with abnormal eicosanoid metabolism then disturbed platelet function may be observed. We have measured platelet aggregation (PAG) at 37°C to ADP (8 1:1 sequential dilutions from 10μM), collagen (2mg/l) and adrenaline (5μM) in 37 patients with Raynaud's syndrome (21 primary (RD), 9 secondary to scleroderma (RP) and 7 vibration white finger disease (VWF)) and 10 normal subjects (N). In addition we have determined the platelet aggregate ratio (PAR). PAG was expressed as the percentage fall in optical density after the addition of the aggregant. We also recorded the duration of the collagen lag phase and the concentration of ADP at which disaggregation occurred (DAC).

	Collagen	ADP 3min 2.5μM	ADP 3min 1.25μM	DAC	Adrenaline 3min	Adrenaline 5min	PAR
	lag(s)	%agg.	%agg.	(μM)	%agg.	%agg.	
N :	96±30	51±27	52±12	24±27	1.2500	31±25	47±29	0.90±0.10
VWF:	99±33	48±21	42±16	22±22	1.2500	34±18	56±19	0.89±0.07
RD :	74±30	57±18	53±15	35±16	0.6250	46±13	54±16	0.80±0.15
RP :	57±12	61±10	60±15	54±13	0.3125	50±15	65±14	0.81±0.16

Results: Mean±SD. Statistical analysis: Mann-Whitney U test.

Patients with RP showed enhanced PAG compared to normals. This reached significance for collagen lag phase ($p<0.001$), percentage PAG at 3 minutes to ADP 1.25μM ($p<0.05$) and the DAC ($p<0.01$). Similar differences were observed between patients with RP and VWF. Patients with RP also showed significantly enhanced PAG with regard to ADP 1.25μM ($p<0.01$) and the DAC, ($p<0.05$) compared to patients with RD. There was no significant difference in platelet function between normal subjects and patients with VWF or between normal subjects and patients with RD. Only with regard to DAC did patients with RD differ from patients with VWF ($p<0.05$). The differences observed in PAG were not reflected by the PAR. Patients with RP have significantly enhanced PAG when compared to all other groups. This may relate to eicosanoid metabolism and provides a rationale for treatment.

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INCREASED PLATELET AGGREGABILITY IN NATIVE WHOLE BLOOD IN THE ADULT RESPIRATORY DISTRESS SYNDROME (ARDS). I.J. Mackie, D. Bihari, S.J. Machin. Haematology Dept., The Middlesex Hospital, London, W1, UK.

The measurement of aggregation in whole blood allows the study of platelets in their natural milieu, but may still have anticoagulant induced artifacts; citrate decreases extracellular (Ca^{++}) and heparin activates platelets. A technique for measuring aggregation in unanticoagulated (native) whole blood (NWB) was developed; blood is diluted in prewarmed saline with and without platelet agonists and aggregation is monitored by electrical impedance. Spontaneous and collagen induced aggregation were measured and the effect of prostacyclin analogue ZK 36,374 studied. The time until response (lag), aggregation rate, and clotting time were measured. Normal blood gave a cv of <7% for the NWB parameters; collagen gave a shorter lag and higher rate than in citrated whole blood (CWB). The lag and rate were inhibited in a dose dependent manner by ZK 36,374. 6 patients were studied on admission with ARDS and followed for several days. All had increased aggregation to collagen, which was more pronounced in NWB than CWB. A shortened lag was seen in some patients, but none showed spontaneous aggregation. ARDS patients showed no inhibition to ZK 36,374, and the heightened aggregation was not influenced by 2mM ASA, or normal plasma, while 2.5mM EDTA abolished all responses. Serum thromboxane B_2 was normal, and increased flux through the cyclo-oxygenase pathway therefore unlikely. A parallel study has shown very low levels of antithrombin III (ATIII) in these patients, which may mean an increased thrombin generation rate with more thrombin available for platelet activation. This partly explains the difference in degree of hyperaggregability seen with NWB and CWB. During recovery from ARDS, collagen aggregation and the response to ZK 36,374 normalises at the same time as AT-III increases.

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REDUCED THRESHOLD FOR COLLAGEN INDUCED PLATELET AGGREGATION IN WHOLE BLOOD FROM PATIENTS WITH SYSTEMIC SCLEROSIS. M.J.D. Goodfield (1), M.A. Orchard (2), N.R. Rowell (1). Department of Dermatology (1), Department of Medicine (2), General Infirmary at Leeds.

Systemic sclerosis is a multi-system disorder characterised by skin lesions and narrowing of arterioles with reduction in blood supply to many organs. Previous reports have suggested that platelet aggregation is abnormal and could contribute to the pathogenesis. Platelet aggregation in whole blood was investigated in 10 patients with systemic sclerosis and 9 age matched controls. Subjects rested for 30 minutes before blood samples were taken without stasis, via a 19G needle into 3.8% trisodium citrate anti-coagulant. 0.5ml of blood was transferred to cuvettes, and equilibrated at 22°C for 30 minutes, before being stirred at 750 r.p.m. at 37°C. Aggregation was induced by collagen (0.01 ug/l to 1.0 ug/l), adrenaline (0,1,0.5 and 1.0 ug/l) and ADP (0.1,0.25 and 2.5 ug/l). Aliquots for counting free platelets were taken and assessed using the Ultraflow 100 particle counter.

Platelet aggregation was significantly increased in patients with systemic sclerosis at all doses of collagen ($p<0.01$), and the mean dose giving 50% aggregation was significantly lower in the disease group (0.026+/-0.06mg/l) than in the controls (0.23+/-0.06mg/l, $p<0.01$). Aggregation was not significantly different with the other aggregating agents.

Increased sensitivity of platelets to aggregation by collagen in whole blood may be of importance in the pathogenesis of the vascular and fibrotic lesions of this disease

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CHANGES IN PLATELET ACTIVITY, FIBRONECTIN AND TISSUE PLASMINOGEN ACTIVATOR DURING ARTERIOGRAPHY IN PATIENTS WITH ISCHAEMIA EXTREMITIES INFERIES. W. Augustyniak (1), C.S. Cierniewski (2), W. Slawinski (1), J.H. GOCH (1), R. Polanowska (2).IV Department of Internal Disease, Military Medical School (1) and Department of Biophysics, Medical School of Lodz (2), Poland.

Platelets and endothelial cells may be activated to release their contents during arteriography, which is one of the most frequently used examinations of patients with peripheral vascular diseases. This technique involves lumbar aortic puncture and catheterization with administration of contrast medium in arteriosclerosis obliterans (AO) extremities inferies. In this report we have studied 26 patients aged 37 to 73 years with AO who were subjected to arteriography performed according to the Seldinger method. Concentrations of β-thromboglobulin (β-TG), platelet factor 4 (PF4) and plasma fibronectin (Fn) were determined by radioimmunoassay and tissue plasminogen activator (t-PA) activity was measured by a solid-phase fibrinolytic assay using polystyrene test tubes coated with ^{125}I-fibrin. The levels of these parameters were analysed in samples of both the arterial and vein blood which had been taken before and after the injection of contrast medium and obtained results are given in the Table.

	Arterial blood Before	Arterial blood After	Vein blood Before	Vein blood After
β-TG (ng/ml)	46.8±17.9	38.8±13.4	39.3±14.0	50.2±18.6
PF4 (ng/ml)	16.5±4.3	13.6±6.1	14.9±5.1	17.6±6.9
Fn (μg/ml)	486.0±255	392.0±225	425.0±245	391.0±203
t-PA*	156.0±68	208.0±73	256.0±81	264.0±92

* expressed in pmoles of ^{125}I-fibrin/min/ml

Our results suggest that after the injection of contrast medium there is a significant increase in the t-PA activity in the arterial blood and the β-TG concentration in the vein blood.