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Gregorio Caimi was born in Marsala (Sicily). Graduated with honours in Medicine at the University of Palermo in 1969. He did his post-graduate degree in Internal Medicine in Cagliari. Associated Professor since 1984 and Full Professor in Internal Medicine since 2002, he teaches Semeiotics and Clinical Methodology at the School of Medicine of the University of Palermo. In charge of the Laboratory of Clinical Haemorheology in the Department of Internal Medicine, Cardiovascular and Renal Disease of which he is Chair. Since 2007 Caimi is Chair of the post-graduate school of Sports Medicine. From 1992 to 2005 he was the General Secretary of the Italian Society of Clinical Haemorheology and since 2005, is the President of the Italian Society of Clinical Haemorheology and Microcirculation. From 2005 to 2011, Vice-President of the European Society for Clinical Haemorheology and Microcirculation. Since 2012, he is the Pro-Rector of the University of Palermo. Referee for several scientific journals concerning topics in clinical haemorheology. He is a member of the Editorial Board of Clinical Haemorheology and Microcirculation and of the Committee of the European Society for Clinical Haemorheology and Microcirculation.

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Signal transduction pathways in erythrocyte nitric oxide metabolism under high fibrinogen levels

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Fibrinogen is a plasma protein that beyond its hemostatic function behaves as an acute phase protein and as a hemorheological factor. The erythrocyte hyperaggregation state induced by fibrinogen takes place in various metabolic and cardiovascular diseases such as diabetes, arterial hypertension and atherosclerosis. Soluble form of fibrinogen binds to erythrocyte CD47. Soluble thrombomodulin is an inflammatory marker that binds erythrocyte CD47 in a sequence peptide known as 4N1K.

Hiperfibrinogenemia induced *in vitro* modulates erythrocyte nitric oxide (NO) metabolism in dependence of band 3 phosphorylation degree. When in presence the CD47 agonist peptide, 4N1K,and at hiperfibrinogenemia no variations was observed in erythrocyte NO efflux at variance with increased GSNO, peroxinitrite, nitrite and nitrate concentrations.

The aim of this work was to study the influence of the CD47 agonist peptide, 4N1K, on the erythrocyte NO metabolism in the presence of inhibitors of band 3 phosphorylation degree under high fibrinogen concentration.

In this *in-vitro* study, whole blood samples were harvested from healthy subjects and NO, peroxynitrite, nitrite, nitrate and S-nitroglutathione (GSNO) were determined in presence of 4N1K, calpeptine, Syk inhibitor and under high fibrinogen concentrations. The results obtained, when 4N1K is present with either calpeptine or syk inhibitor in presence of high fibrinogen levels show, in relation to control, (1) no variations on the levels the erythrocyte NO efflux; (2) increased concentrations of the reactive nitrogen species namely peroxynitrite *($p<0.05$; $p<0.005$)*, nitrite *($p<0.0001$; $p<0.001$)* and nitrate *($p<0.0001$; $p<0.001$)*; (3) increased GSNO concentrations *($p<0.001$; $p<0,001$)*.

In conclusion the CD47 agonist peptide 4N1K induces erythrocyte NO mobilization in hiperfibrinogenemia independent of erythrocyte membrane band 3 protein phosphorylation status.

Hemorheological parameters profile in children with sickle cell disease

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Patients with sickle cell disease (SCD) have intermittent painful crises caused by recurrent vaso-occlusion in microcirculation resulting from sickle red blood cells (SS-RBCs) adhesion to endothelium. Microvascular occlusion is a complex multifactorial process showing alterations in coagulation system, endothelial function and inflammation. Fibrinogen is an acute phase protein and is a major determinant of whole blood viscosity promoting erythrocyte aggregation. The blood rheology contribution to the SCD in children's are poorly studied.

The aim of this study was to evaluate the hemorheological parameters namely erythrocyte deformability (ED) and aggregation (EA), hematocrit, whole blood viscosity (WBV), fibrinogen and their associations with steady--state to vaso-occlusive crisis transitions in children's with SCD.

Thirteen eight SCD patients with age 9,5±4,8 years old have been enrolled and divided in two groups mild (N=28) and moderate/severe (N=3) according the Pediatric Severity Score (PSS). The majority of the patients are in steady state (N=32).

Hemoglobin (Hb), metahemoglobin (MetHb) and carboxihemoglobin (COHb) were determined in a Hemoximeter and the hematocrit measured in a microcentrifuge. EA and ED were assessed using the MA1 aggregometer and the Rheodyn SSD laser difractometer respectively. Whole-blood viscosity were measured with a rotation digital viscosimeter from Brookfield and fibrinogen concentration evaluated in a Fibrintimer, using a modification of the Clauss method. The haematological, biochemical and haemorheological parameters obtained were analysed using EXCELL SPSS 19.0.

Concerning all patients the results showed decreased values of Hb and hematocrit; increased values of MetHb in crisis; higher fibrinogen values were associated in the higher MetHb quartile; increased erythrocyte COHb levels is negative associated with haemoglobin (r=-0.502; p=0.001) and positively associated with higher MetHb quartile. Lower values of MetHb are associated with higher EA quartile. Lower values of COHb are associated with higher ED quartile. High values of erythrocyte deformability, in crisis, were verified at low shear stress. The ED values obtained at 6.0 Pa and 30.0 Pa are directly associated (r=0.644, p=0.000; r=0.517, p=0.001, respectively) with hematocrit; higher values of ED are associated with higher EA quartile. Lower reticulocytes number is associated with WBV higher quartile.

In conclusion the results suggested an oxidative stress environment, exaggerated carbon monoxide production by vascular endothelium hemoxigenase, which is a marker of endothelial dysfunction. The intravascular hemolysis that occur in these patients may be the cause of the increased of hemoxigenase enzyme activity. The improvement of ED in lower shear stress may be the results of less constraint applied favouring lower release of oxygen and less deoxygenated SS-RBCs.

Erythrocyte Nitric Oxide Association with Low Grade Inflammation

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Atherogenesis is present in patients with systemic lupus erythematosus (SLE) and patients with rheumatoid arthritis (RA) which are at increased risk for vascular disease. Cross-sectional clinical studies performed in patients with atherothrombotic risk factors evidenced associations between erythrocyte aggregation (EA) and those risk factors. The low-grade inflammation verified in patients with atherothrombotic risk factors shows that fibrinogen mediates erythrocyte hyperaggregation. Previously we have showed increase erythrocyte nitric oxide (NO) efflux ability in blood samples from patients with vascular disease namely atherosclerosis, hypertension and erectile dysfunction.

The aim of this study was to evaluate in SLE and RA patients the erythrocyte NO biovailability and to examine its association with EA and subclinical atherosclerosis.

The 197 women patients (96 SLE and 101 RA) were enrolled and compared with 97 controls and carotid intima-media thickness (cIMT) evaluated (using ultrasonography Philips-ATL HDI 5000) as well as erythrocyte NO (using the aminoNO-IV sensor) and EA (by MA1 aggregometer from Myrenne GMBH)

The results showed increase EA in SLE and RA patients compared with controls being higher when in patients are in active state. The multivariable analysis showed associations between EA with cardiovascular and inflammatory risk factors and erythrocyte NO production is negatively associated with cIMT.

Both SLE and RA are systemic rheumatic inflammatory diseases associated with sub-clinical atherosclerosis.The increase EA may contribute to endothelium dysfunction but the erythrocyte NO scavenger ability verified in both group of patients may reduce the NO produced by endothelial inducible nitric oxide.

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Effects of fibrinogen in mice leukocyte recruitment

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In vitro soluble fibrinogen (sFib) modulate leukocyte adhesion to endothelium. This rise the question that In vivo sFib may influence leukocyte recruitment. To address this question under absence of sFIb acute inflammation was performed in mice (Fib alpha -/-), by perfusing PAF over mesentery exposed in an intravital microscopy. Two types of mice wild and heterozygous were used. Under acute inflammatory conditions an abnormal pattern of recruitment was observed for leukocytes in homozygous (sFib alpha -/-) in comparation with both control groups. The leukocyte recruitment in homozygous mice is compromised suggesting a role of fibrinogen in leukocyte recruitment in inflammation.