O7: Disease and Hemorheology - 1

O7-1 Do changes in bone marrow pressure contribute to the egress of cells (RBC,RETICUL.) from bone marrow?

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Pressure was measured in the femoral medullary cavity of rabbits whose femoral muscles were subjected to electrostimulation. After electrostimulation the pressure in the medullary cavity increased fivefold. In groups of experimental animals the number of reticulocytes leavin the bone marrow and the number of reticulocytes in the peripheral blood were determined and it was observed the electrostimulation was followed by a severalfold rise in the amount of reticulocytes in both the bone marrow and the peripheral blood. The authors found that great role in the egress of reticulocytes from the bone marrow into the circulation is played by regulation of the pressure in medullary cavity effected by changes in blood flow trough the bone marrow.

O7-2 Platelet-derived extracellular vesicles promote the adhesion of flowing neutrophils to endothelial cells

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Activation of platelets causes them to shed numerous extracellular vesicles (PEV) which may have inflammatory effects. We tested the ability of PEV to promote adhesion of flowing neutrophils to endothelial cells (EC), and the separate contributions of PEV subpopulations, platelet membrane microvesicles (PMV) and exosomes (Pexo). PEV were collected from platelets stimulated with collagen-related peptide, and PMV and Pexo were separated by differential centrifugation. Vesicle binding and resultant activation of neutrophils and EC were assessed by flow cytometry. Flow-based adhesion assays assessed binding of neutrophils directly to deposited vesicles or to EC, after neutrophils or EC had been treated with vesicles. In suspension, PEV bound efficiently to neutrophils or EC, with resultant upregulation of activation markers on both types of cell. Binding was Ca^{++}-dependent, and dominantly mediated by CD62P for neutrophils, or by integrins for EC. When PEV were deposited on surfaces of flow chambers, they supported mainly short-lived attachments of flowing neutrophils through CD62P, and some stable adhesion induced by CXC-chemokines. Neutrophil adhesion to EC was promoted when either cell was pre-treated with PEV, although the effect was less prominent when EC were pre-activated with tumor necrosis factor-α. The pro-adhesive effects on neutrophils could largely be attributed to PMV rather than Pexo. Thus, surface-bound PEV can capture flowing neutrophils, while PEV also activate neutrophils and EC to promote interactions. PEV may potentiate inflammatory responses (thromboinflammation) after platelets are activated in tissue injury.

O7-3 Morphological and Metabolic Abnormalities of Erythrocytes as Risk Factors for Alzheimer's Disease

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Alzheimer's disease (AD) is the most common form of dementia, that affects about 30 million people worldwide. The first step towards this whole-scale problem is to keep on studies of a new model based on red blood cells (RBC) interaction with amyloid beta 1-42 peptide (Aβ). RBC are highly deformable to assist blood flow in the microcirculation and for this reason morphological and functional abnormalities in RBC could contribute to AD by obstructing oxygen delivery to brain causing hypoxia. We show that treatment with Ab accelerates the occurrence of morphological and biochemical aging markers in human RBC and influences the cell metabolism. The morphological pattern has been monitored using AFM imaging. Results evidence that Ab boosts the development of crenatures and proto-spicules simultaneously to acceleration in the weakening of the cell-cytoskeleton contacts and to the induction of peculiar nanoscale features on the cell membrane. Incubation in the presence of glucose can remove all but the latter Ab-induced effects. Biochemical data demonstrate that contemporaneously to morphological and structural alterations, Aβ trigger: (i) metabolic and antioxidant defense alterations and (ii) a complex signaling pathway involving membrane Acetylcholinesterase, caspase 3, protein kinase C and nitric oxide derived metabolites. Our study provides a comprehensive picture in which Aβ treatment of RBC induces changes in specific cell signalling events and/or metabolic pathways, in turns affecting the membrane–cytoskeleton interaction and the membrane integrity. Understanding these processes is highly relevant for the comprehension of the biochemical events which predispose to AD.

O7-4 Effects of two different high intensity interval training protocols on hemorheological variables in hypertensive patients

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Purpose: The present study examined and compared the effects of two different HIIT protocols on markers of blood fluidity in hypertensive patients. Methods: Thirty hypertensive (stage 1, systolic BP >140 and diastolic BP>90 mmHg) patients (age, 47.96±3.20 yrs), were randomly allocated to short duration HIIT (SDHIIT, n=10), long duration HIIT (LDHIIT, n=10), and control (n=10) groups. After two weeks of continuous mild training, patients in SDHIIT group performed 8 weeks of HIIT included 27 min HIIT that encompassed 27 repetitions of 30s activity at 80%-100% of VO_{2peak} interspersed by 30s passive/active (10%-20% of VO_{2peak}) recovery, while, patients in LDHIIT group performed 8 weeks of HIIT (32min per session) included 4 repetitions of 4min activity at 75%-90% of VO_{2peak} interspersed by 4min passive/active (15%-30% of VO_{2peak}) recovery. Two blood samples were taken before and after training and were analyzed for hemorheological variables. Results: Significant ($P<0.05$) reductions in systolic blood pressure (SBP), blood and plasma viscosity, fibrinogen concentration, and red blood cell (RBC) aggregation were found following two training protocols, though, the differences between the two training protocols

were not statistically significant. Conclusions: It is concluded that HIIT training reduces SBP and markers of blood fluidity in patients with stage 1 hypertension irrespective of the HIIT intensity and duration.

O7-5 Sedentarity status as a regulator of the optimal hematocrit: involvement of red cell deformability?

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We recently proposed to calculate a "theoretical optimal hematocrit" as the value associated with the higher value of hematocrit/viscosity (h/η) on the bell-shaped curve predicted with Quemada's equation (viscometry at 1000 s^{-1}). We reported that this approach provides values of optimal hematocrit and h/η well correlated with the actual values, but closer to them in well trained athletes and higher than them in sedentary and obese individuals. Applying this model to several databases used in our previous studies we confirm that obese subjects with or without metabolic disturbances exhibit a higher discrepancy between actual and « predicted ideal » values of hematocrit and h/η, and that this discrepancy is not related to the level of insulin sensitivity. By contrast this discrepancy is well correlated with red cell rigidity. In sedentary patients with the metabolic syndrome 3 months of regular low intensity exercise training shifted the bell-shaped curve of predicted h/η toward higher values ($p<0.01$). Therefore, sedentarity seems to shift hematocrit and h/η toward values lower than the theoretical optimal ones while exercise training decreases this discrepancy. This mechanism is not related to insulin resistance but correlated with red cell rigidity. It may reflect an adaptative mechanism allowing to maintain an optimal oxygen supply during exercise in sedentary individuals whose hemorheological profile is impaired.

O7-6 The effects of n-6 polyunsaturated free fatty acids dietary intake on hemorheology and endothelium-dependent microvascular function

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Potential beneficiary effects of dietary or supplementary daily intake of n-3 polyunsaturated fatty acids (n-3 PUFAs), such as α‑linolenic fatty acid, eicosapentaenoic acid, and docosahexaenoic acid on hemorheology and vascular function are currently intensively investigated. Depending on the source of n-3 PUFAs and the study subjects (i.e. healthy individuals or cardiovascular patients) n-3 PUFA supplementation have been shown to have the antitrombotic effects (by decreasing blood viscosity, decreasing FIIc, FIXc, FXc, FVIIc, FVIIa, FXIIa, PAI-1 levels and platelet aggregation/reactivity, enhancing fibrinolysis, but

without effects on erythrocyte deformability). They decrease inflammation by decreasing IL-6, MCP-1, TNF-alpha and hsCRP levels, expression of endothelial cell adhesion molecules and significantly affect blood composition of fatty acids.

It is well accepted that the metabolites of n-6 PUFA, such as the metabolites of arachidonic acid have very important role in many physiological processes in cardiovascular system.On the other hand, there are controversies in the beneficial effects of n-3 PUFAs consumption on macrovascular function, and studies on microvascular function are rare.Recently we have showed significantly enhanced endothelium-dependent microvascular reactivity to reactive hyperemia in young healthy population. Plasma hsCRP and lipid peroxidation products were decreased and antioxidative enzymes function was enhanced (i.e. increased glutathione peroxidase activity). The possible underlying protective mechanisms of n-3 PUFA intake may be a change in balance of n-6 PUFA metabolites (e.g. prostaglandins and leukotrienes) and n-6 PUFA metabolites (such as resolvins, maresins and protectins), reduced inflammation and decreased vascular oxidative stress