So, B cell compartment of the offspring of centenarians seems to be more similar to that of young respect to the old one. B cell subset changes could represent a hallmark of immunosenescence and could be used as a biomarker of human life span, potentially useful for the evaluation of anti-ageing treatment.

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PROTHROMBOTIC VARIANTS IN ELDERLY

G. Chiarello, L. Liga, C. Migliorisi, B. Lo Sasso, M. Ciaccio

Chair of Clinical Biochemistry, School of Medicine, University of Palermo, Italy

Venous thrombosis is a common disorder in the elderly with a substantial morbidity and mortality. Environmental risk factors, particularly immobilization, play an important role in the etiology of thrombosis in the elderly, and cause a substantial proportion of the total number of cases because risk factors associated with disease are more prevalent in old than in young individuals. Abnormalities in the clotting system, either genetic or acquired, appear to be equally and possibly more important in the elderly than in young and middle-aged individuals (1). Thrombosis results from the interaction between predisposing genetic polymorphisms and acquired risk factors (2). Knowledge about hereditary thrombophilia has increased in the last two decades and this has lead to widespread testing of hereditary thrombophilia in patients with venous thromboembolism. Several allelic variants have been associated with inherited thrombophilia, these include: factor V Leiden, factor II Prothrombin G20210A, beta-fibrinogen -455G>A, methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C, plasminogen activator inhibitor-1 (PAI-1) 4G/5G, Apolipoprotein E (Apo E) polymorphisms, angiotensin converting enzyme (ACE) I/D (3-4). Variants of certain haemostatic genes (such as that encoding factor V Leiden) are involved in the development of venous thrombosis (5). The risk of venous thrombosis associated with factor V Leiden increases when other thrombophilic genes co-exist and when acquired risk factors are also present (6). The second most common form of reported inherited thrombophilia is the prothrombin polymorphism G20210. This mutation increases the concentration of circulating prothrombin. MTHFR catalyzes remethylation of homocysteine to methionine. Elevated levels of homocysteine can result from several mutations in the MTHFR gene (C677T and A1298C) and have been identified as risk factors for thrombosis (7). A defective fibrinolysis can also contribute to thrombosis and patients with a history of thrombosis were found to have a high prevalence of increased plasminogen-activator 1 (PAI-1) levels (8). Yet there are few data in the literature about the prevalence of these polymorphisms in the centenarian population.

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FETUIN-A, RENAL FUNCTION AND CARDIOVASCULAR DISEASE IN ELDERLY SUBJECTS

C. Bellia, A. Caruso, S. Cammarieri, R. Carollo, M. Ciaccio

Chair of Clinical Biochemistry, School of Medicine, University of Palermo

Because human serum is supersaturated with respect to calcium and phosphorus, the existence of serum-based precipitation inhibitors has long been postulated. Human fetuin-A, also known as alpha2-Heremand Schmid glycoprotein, a protein produced by the liver and secreted into serum in high concentrations, about 0.5-1.0 g/l, is a major serum-based inhibitor of vascular calcification and accounts for roughly 50% of the inhibition of calcium and phosphorus precipitation (1). In fetuin-deficient mice, the serum inhibition of apatite formation was compromised as well as in heterozygotes. In addition, homozygous fetuin-deficient developed ectopic microcalcifications in soft tissues (2). After these seminal evidences, it has been demonstrated that precipitation inhibition by fetuin-A is caused by transient formation of soluble, colloidal spheres, containing fetuin-A, calcium and phosphates, providing a possible way to transport and remove mineral precipitates in the bodies of mammals (3, 4). Moreover, patients with end-stage renal disease and chronic kidney disease usually have lower serum levels than age- and sex-matched populations with normal kidney function (5), providing a physiopathological link between kidney dysfunction and the higher prevalence of cardiovascular disease observed in these patients. Further evidences supporting this hypothesis came from the study of Moe et al that shown a negative correlation of coronary artery calcification scores, assessed by computed tomography, with serum fetuin-A levels; moreover, authors demonstrated an increased immunostaining for fetuin-A in arteries with increasing calcification (6). Several evidences indicate that the role of fetuin-A in renal and cardiovascular disease may be more complex: actually, in a cohort of coronary artery disease patients, Ix et al found a direct correlation between higher cystatin C, which indicates a worse kidney function, and adjusted mean serum fetuin-A concentrations (7). In addition, it has been recently demonstrated that higher fetuin-A levels confer a higher risk of myocardial infarction and ischemic stroke in the general population (8). Moreover, there are no data regarding circulating levels of fetuin-A in elderly and their potential association with renal function, which notably declines during aging.

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