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Atherosclerosis –

so well-known and still mysterious

Atherosclerosis has drawn attention of researchers, scientists and physicians for far more than hundred years and it would be very difficult to find a subject of medical focus with greater amount of evidence than atherosclerosis and related vascular disease. And this is very much right. Despite all the years and many substantial achievements in the identification of atherosclerosis triggers and factors of progression we still witness atherosclerotic vascular events topping mortality and morbidity statistics in the developed world. And as in every topic with intensive research activity the debate on the importance of both the newly identified and the old, established risk factors of atherotrombotic vascular disease is still hot and excited. European Atherosclerosis Society in a close cooperation with its national counterparts creates an ideal arena for such a debate which annual highlight takes place at the EAS congress – this year being hosted by the Czech Society for Atherosclerosis in the beautiful city of Prague. On this very special occasion we have prepared a selection of literature from leading Czech research groups looking at atherosclerosis from different angles.

We believe there are some common grounds on which we can support our understanding of the pathogenesis of atherosclerotic vascular changes. The primary culprit in this respect seems to be the delivery of lipids into the subendothelial layers of arterial wall by atherogenic lipoproteins. We have a vast evidence supporting this notion and one of its primary level comes from the experience with diseases characterized by marked accumulation of apolipoprotein B containing particles in the plasma due to a well-established genetic defect – autosomal dominant hypercholesterolemia or familial hypercholesterolemia (FH). Our appreciation of the disease has grown markedly since its first description and we know a lot more even in comparison with recent times, when the first studies on its molecular-genetic background were published. Given FH has become a flagship of both research and clinical lipidology one does not find it surprising we dedicate a substantial space of this supplement to FH starting from the importance and organization of screening programs and characteristics of FH individuals in the current times to the recent expansion of our understanding of the molecular signature of FH (which is no more a simple monogenic disease) to explaining the phenotypic variability of the FH patients by detailed gene profiling. This includes the recently intensively studied posttranslational modification and the role of miRNA with a substantial modulating impact on CVD risk and atherosclerosis progression in different models and populations.

Sometimes conflicting findings of observational, epidemiological, animal and *in vitro* studies are a matter of ongoing discussions. And we have included just another piece of the puzzle to this supplement. Total cholesterol did not prove to be a significant predictor of CVD risk in four male cohorts as reported by Hubacek *et al*. There might be a number of explanations of this, at a first sight, surprising observation. We would not substitute the authors and discuss their results but rather point to other works in this issue that shall guide our way of evaluating such results. While we have learned a lot on the risk factors for atherosclerosis (also thanks to huge evidence gathered in animal experiments as nicely reviewed by Poledne and Jurcikova-Novotna in this issue) there is relatively little known on putative protective factors slowing down or even halting atherogenesis. As an example, we may consider the story of bilirubin and its role in the development of vascular damage as summarized by Vitek. Of course, given the very complex and multifaceted pathophysiology of atherosclerosis, we have to employ much broader approach when analyzing the observed differences between cases and controls or between different populations. Inclusion of novel biomarkers may help us in some situations: Kraml´s review on the role of iron in the development of atherosclerosis may serve as

a suitable example. Even some well-established risk factors like lipoprotein (a) have not been fully understood and their new roles in vascular damage are being discovered (see the review by Vaverkova *et al.*). Another aspect of sometimes puzzling results of different studies might be the timing of evaluation – as we are reminded in a thoughtful review by Pitha – a lot can be lost in the menopausal transition with regards to cardiovascular health.

After all, let me close this Introduction in a positive tone. Rosolova *et al.* have summarized the three decades´ results of cardiovascular prevention efforts as assessed in the Czech part of the EUROASPIRE surveys. And despite there is a relatively large room for improvement, a lot has already been achieved. These results are a combination of population attributable risk changes and individual management of very high risk individuals. From the population perspective we appreciate the fundamental role of lifestyle changes and interventions in this direction represent important strategy to achieve maximum risk reduction, as described by Mraz *et al.* in their original contribution to the issue. The other edge of intervention that changes the prognosis of our patients is being represented by aggressive treatment methods like lipoprotein apheresis, which lead us back to the topic of familial hypercholesterolemia. Lipoprotein apheresis is a method of choice for homozygous FH patients but has a potential benefit to a much broader patient population (see the contribution of Blaha *et al.*).

Let us hope the progress in our understanding of the underlying causes of atherosclerosis will continue and we will be able to gradually disclose more mysteries in the pathogenesis of atherosclerotic vascular disease. Obviously, we would not be able to proceed to this end without collaboration and joined forces. Thus, international collaboration platforms as provided by the European Atherosclerosis Society are of great importance. On behalf of many colleagues who devoted time and effort to the organization, it is my personal pleasure to welcome you to the 85th Congress of the European Atherosclerosis Society also with this Supplement of *Physiological Research* and wish you to enjoy its professional as well as social interactive parts to achieve our mutual goal – better understanding of atherosclerotic vascular disease and the ways to defeat it.

Michal Vrablik
85th EAS Congress Chair
Chairman of the Czech Society for Atherosclerosis