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Evaluation of Ph.D thesis entitled: „Interactive influences of enviromental and genetic factors on the properties of large arteries in relation to sodium handling“

General evaluation:

This thesis entitled interactive influences of enviromental and genetic factors on the properties of large arteries in relation to sodium handling aimed at the potential relationship between properties of large arteries, renal sodium handling and candidate genes encoding renin-angiotensin -aldosterone system and adducin. This project is part of the large international EPOGH study.

Thesis addresses important issues: the potential differences in arterial properties/mainly arterial stiffness/ in normotensive offspring of parents with or without hypertension. Normotensive offspring of hypertensive parents had altered large artery properties compared to normotensive offspring of normotensive parents. The major determinant of these differences was high blood pressure.

Thesis contains also original data concerning the heritability and familial agregation of various indexes of arterial stiffness. The authors found significant correlation between genetic background and aortic stiffness. Higher fractional sodium reabsorption in the distal nephron is associated with higher compliance and distensibility of femoral artery, while higher proximal sodium reabsorption leads to the opposite results. These results are in concordance with the pathophysiological view of the influence of high sodium intake on arterial properties/blood pressure. In addition to that, these results corresponds to the findings in some secondary form of hypertension/primary aldo/.

The authors concentrated also on the potential association between arterial properties and genes encoding alpha-adducin (ADD). Brachial artery properties were related to ADD3 polymorphism. Interaction between ADD and angiotensin converting enzyme in relation to arterial properties was also studied. Brachial diameter was increased in ACE CG haplotype homozygotes compared with non-carriers.

The total evaluation of the thesis from my site is extremely positive.

Major comments:

The thesis is well and clearly written, the methodology used is sufficient and appropriate. Most of the results were obtained on the relatively large group of subjects in different European countries which increases the quality and reproducibility of the work. Also statistical approach is based on appropriate tests.

All thesis has 175 pages and its structure is based on the already published results in peer-reviewed international journals / 5 publication of dr. Seidlerova as a first author and 4 publication as a co-author who significantly contributed to the published results. All these 9 articles were published in journals with high impact factor, which makes all review process more easy.

Prof. Dr. Jiri Widimsky jr Ph.D, Prague, July 20, 2009

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