XXIX JCET LECTURE, 31.01.2014, 9.00

Structure of small arteries: endeavours in translation

Prof. Michael J. Mulvany
Department of Biomedicine, Aarhus University,
Aarhus, Denmark

Essential hypertension is treated primarily with a view to reducing blood pressure, and not with regard to normalizing the main pathological changes: the peripheral resistance and the cardiovascular structure. The aim of this communication is first to review how the author came to consider this question – which is a lesson in serendipity. Second, to discuss whether normalization of small artery structure may also be a target for therapy. The following points will be presented. Firstly, the evidence that altered structure of the resistance vasculature, an increase in the media:lumen ratio of the vessels, is due to inward eutrophic remodelling (reduction in lumen without change in wall mass). Secondly, the evidence that it may be possible to rectify the abnormal structure, where it appears that this requires a therapy which causes vasodilatation in the individual concerned. Thirdly, the evidence that altered small artery structure appears to have prognostic consequences. Fourthly, the cellular mechanisms which

may be involved, where available data indicate that vasoconstriction in itself can cause inward remodelling, and that this can be prevented by vasodilators. The enzyme tissue transglutaminase (type 2 transglutaminase) appears to be involved, and inhibition of this enzyme can inhibit remodelling. Finally, the evidence that these findings may provide clues for strategies that may be able to improve the outcome of antihypertensive therapy. Taken together it may be concluded that there is reasonably strong evidence that a treatment which reduces peripheral resistance in the individual patient will, apart from reducing blood pressure, also improve the abnormal structure. However, the prognostic implications for this remain unknown.

CURRICULUM VITAE

Prof. Michael J. Mulvany

Current title: Professor emeritus, Department of Biomedicine

Aarhus University, Aarhus, Denmark. mm@farm.au.dk

Qualifications

1962 Honours degree in Mathematics and Engineering Science, Oxford, UK.
1978 Licentiate (PhD) in Biophysics, University of Aarhus.

1983 Doctor of Medical Sciences (DMSc) in Biophysics, University of Aarhus.

Positions

1969-2011 Assistant/Associate Professor/Professor, Dept. Biomedicine, Aarhus University, DK.

1974-76 Research Associate, Dept. Physiology, University of Vermont, Vermont, USA.

2011- Professor Emeritus, Dept. Biomedicine, Aarhus University

Scientific work

Structure and function of small arteries and their role in the development of high blood presure (hypertension). Major work: (a) Structure and function of small arteries. (b) Investigation of abnormal structure of small arteries in hypertension; (c) Drug treatments which can normalize the abnormal structure. Ca. 300 publications, H-index 60.

Experience with doctoral training

2003-2010 Head, Aarhus Graduate School of Health Sciences

2011-2013 Consultant, Aarhus Graduate School of Health Sciences

2005-2012 Representative for Faculty of Health Sciences, Aarhus University in Organization for PhD education for PhD education in biomedicine and health sciences in the European system (ORPHEUS).

2010- Vice-president ORPHEUS.

Selected assignments

2000-2007 Chairman, Danish Society of Pharmacology and Toxicology

2006-2012 Member of EPHAR executive council

2001-2010 Secretary-General World Congress of Basic and Clinical Pharmacology 2010 (IUPHAR2010), Copenhagen

Selected prizes

2002 Malpighi award, European Society of Microcirculation

2013 BCPT Nordic prize in Basic and Clinical Pharmacology

Publications

Cited by Medline total 259 (49 since 2003). In addition ca. 60 book chapters, and supplements. H-index 60.

Selection:

Mulvany MJ, Halpern W: Mechanical properties of vascular smooth muscle cells in situ. Nature 1976,260:617-619.

Aalkjaer C, Heagerty AM, Petersen KK, Swales JD, Mulvany MJ: Evidence for increased media thickness, increased neuronal amine uptake, and depressed excitation-contraction coupling in isolated resistance vessels from essential hypertensives. Circ Res 1987,61:181-186.

Mulvany MJ, Aalkjær C: Structure and function of small arteries. Physiol Rev. 1990, 70: 921-961.

Thybo NK, Stephen N, Cooper A, Aalkjær C, Heagerty AM, Mulvany MJ. Effect of antihypertensive treatment on small arteries of patients with previously untreated essential hypertension. Hypertension 1995; 25: 474-481.

Simonsen U, Wadsworth RM, Buus NH, Mulvany MJ. In vitro simultaneous measurements of relaxation and nitric oxide concentration in rat superior mesenteric artery. J Physiol 1999, 516.1, 271-282.

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Mathiassen ON, Buus NH, Sihm I, Thybo NK, Morn B, Schroeder AP, Thygesen K, Aalkjaer C, Lederballe O, Mulvany MJ, Christensen KL: Small artery structure is an independent predictor of cardiovascular events in essential hypertension. J Hypertens 2007;25:1021-1026.

Skov K, Eiskjaer H, Hansen HE, Madsen JK, Kvist S, Mulvany MJ: Treatment of Young Subjects at High Familial Risk of Future Hypertension With an Angiotensin-Receptor Blocker. Hypertension 2007; 50: 89-95.

Ostergaard L, Stankevicius E, Andersen MR, Eskildsen-Helmond Y, Ledet T, Mulvany MJ, Simonsen U.Diminished NO release in chronic hypoxic human endothelial cells. Am J Physiol 2007; Epub ahead of print.

Jacobsen JC, Mulvany MJ, Holstein-Rathlou NH. A mechanism for arteriolar remodeling based on maintenance of smooth muscle cell activation. Am J Physiol Regul Integr Comp Physiol. 2008; 294: R1379-1389..

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