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LETTER TO THE EDITOR

Heart Failure – the Reason for or a Consequence of Failure of the Periphery?

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The generally accepted concept of failing heart is that peripheral tissues suffer from hypoperfusion resulting in deterioration of life quality and expectancy. Compensatory mechanisms come into operation aiming to restore the relative balance between metabolic needs and blood supply of the periphery and in late periods of heart failure just to save the life (Šimko 1995).

The principal question arises: which mechanisms can reveal that the fully compensated dysfunctional heart is actually failing? The answer is far from being clear, but the nature of the double edged sword of the activated endocrine system might be of substantial importance. The circulatory renin-angiotensin-aldosterone-system (RAAS) and sympathetic nervous system improve the contractility of the heart, maintain the circulating volume of blood and its redistribution. However, besides systemic endocrine activation also local RAAS in the heart, kidney, brain and vessel wall in many organs becomes activated. It is probably stimulated in acute haemodynamic stress but its biological effect is supposed to become manifested especially during a stabilized-compensated haemodynamic situation. There are distinct opinions on the role of this local RAAS. These autocrine-paracrine systems may contribute to proliferative changes resulting in myocardial and vessel wall hypertrophy (Dzau 1992). The hypertrophy of the heart, however, is only the top of the floe; more secrets remain hidden (Šimko 1994, 1996). In the hypertrophied and failing heart the genetic expression is altered resulting in more foetal-like genetic phenotype with depressed expression of sarcoplasmic reticulum ATPase. It is linked with labile calcium homeostasis and danger of myocyte calcium overload (Drexler 1994).

Similarly, undesirable alterations based on the activation of local RAAS may take place in other systems. It does not seem unrealistic to speculate that these extracardial alterations may be at least partially responsible for the shift from compensated myocardial dysfunction to decompensated heart failure. When angiotensin II is excessively formed in the kidney during chronic heart failure, it may result in proliferation of mesangium, proteinuria and deterioration of renal function with fluid retention resulting in additional haemodynamic load stressing further the heart. Angiotensin II produced locally in the brain may lead to the alteration of cardiovascular system regulation, e.g. through an excessive response to common stimuli or insufficient reactions to stress situations. Vascular RAAS is also stimulated during heart failure resulting in downregulation of the endothelial release of nitric oxide and other vasodilating substances. Nitric oxide is not only potentially an antiproliferative and antiatherosclerotic factor. It is believed to be continuously released into the circulation in order to counterbalance the vasoconstricting effect of catecholamines and angiotensin II preserving thus adequate organ perfusion and arterial blood pressure. The lack of NO production may contribute to deleterious rebuilding of the heart and vessels (Bernátová *et al.* 1996), to deterioration of muscle perfusion and enhancement of haemodynamic stress of the failing heart by increasing pre- and after-load.

It is apparent that the triggering issue of heart failure is the disturbance of heart function itself. However, during the compensated period of heart

failure the rebuilding of structure and alteration of function of many organs occur in dependence on the activation of the local RAAS system. Although we do not definitely understand how the changes in peripheral tissues may influence the heart, it is becoming evident that the mutual heart-periphery interplay is much closer than has ever been anticipated.

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