EDITORIAL/VAN DIE REDAKSIE

Association of South Africa and the official departmental hierarchy, to improve the conditions of service of medical superintendents. The latter endeavour has to date failed to achieve its objective.

There *is* a lack of managerial expertise in the public health services of this country. This is not surprising, as South Africa on the whole suffers from a dearth of these essential skills. In the public health services, the causes are multifactorial and obvious. The lack of recognition and reward for medical administrators and the lack of appropriate training courses are obvious. Additional factors include the cumbersome and unwieldy systems and structures imposed by a plethora of public service regulations and controls; financial management and information systems which hinder rather than facilitate good management; personnel management systems which have not adapted to the realities and pressures of the last decade of the 20th century; and the excessive centralisation of control that counteracts the most enthusiastic efforts of those wishing to improve efficiency and effectiveness.

As academic hospitals move towards a new era of greater autonomy, within an academic complex, some of these obstacles will be removed. If, however, medical superintendents are not encouraged, recognised and rewarded, young, dedicated and enthusiastic doctors with management qualifications and experience will become disheartened and discouraged and seek greener pastures in other fields. The loss of this expertise will be detrimental to the future of the health services in general and to academic hospitals in particular. It is in the best interests of the health services and hospitals, of staff and of patients, that every effort be made, not only to retain the medical administrator but to nurture and strengthen the growth of this discipline. Responsibility for this rests with all who desire the emergence of a strong, well-managed and ethically sound health care system in the new South Africa. The matter requires immediate attention and rectification.

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1. Berwick DM, Enthoven A, Beukes JP. Quality management in the NHS: the doctor's role II. *BMJ* 1992; **304:** 304-308.
2. Mintzberg H. *The Structuring of Organisations. A Synthesis of the Research.* Englewood Cliffs, NJ: Prentice-Hall, 1979.

New emphasis on atrial cardiology

Based on the concept that the cardiac muscle is differentiated mainly for excitation, conduction and contraction, cardiology has for many years focused mainly on the ventricles, with comparatively little attention to the atria. However, demonstration of the heart as an endocrine organ and recognition of its role in the regulation of volume and electrolyte homeostasis via the release of the atrial natriuretic peptide (ANP), have led to renewed interest in the atria and emergence of a new research direction, atrial cardiology.

Although it is well established that the atria and ventricles of the mammalian heart differ considerably in their ultrastructure,[1] contractile activity,[2] glycogen content[3] as well as in their response to oxygen deficiency,[4] recent studies have highlighted several other marked differences. Of particular interest is the renin-angiotensin system, the presence of ANP, and the activity of the phosphatidylinositol (PI) signal transduction pathway.

There is now conclusive evidence for the existence of a local intracardiac renin-angiotensin system which produces biologically active peptides via local catalytic pathways.[5] Angiotensinogen gene expression[6] and concentration,[7] the activity of the angiotensin-converting enzyme,[8] the concentration of both angiotensin I and II,[7,9] as well as the binding capacity of angiotensin II receptors[10] have been reported to be higher in the atria than in the ventricles. Although there still is no direct evidence that the cardiac renin-angiotensin system affects cardiac function under normal conditions, there are indications that this system may be involved in several pathological states, i.e. myocardial ischaemia, congestive heart failure, reperfusion arrhythmias and the stunned myocardium (for review see Lindpainter and Ganten[5]).

Although ANP can also be secreted from the ventricles during volume overloading,[11] it is generally accepted that the atria are the major source of this hormone.[12] Atrial stretch[13] and increased heart rate are major inducers of ANP release,[14,15] with the possibility of calcium being the ultimate signal.[11] Other substances which cause ANP release are the potent vasoconstrictor peptide, endothelin,[16,17] and the pressor hormones, angiotensin II and vasopressin.[18]

It is well established that release of ANP from atria has properties beneficial to the circulation in congestive heart failure due to its diuretic and vasodilatory[19] actions as well as its inhibition of aldosterone secretion and antagonism to angiotensin II.[20] However, these beneficial effects of increased ANP levels during congestive heart failure are often overridden by the drive to vasoconstriction and sodium retention resulting from renin-angiotensin aldosterone activation beyond the effective range of ANP.[12]

The activation of a wide range of receptors which employ Ca^{2+} as one of their intracellular signals is associated with stimulation of the PI signal transduction pathway.[21] In the heart activation of either α_1-adrenoreceptors or muscarinic receptors as well as post-ischaemic reperfusion have been shown to stimulate PI metabolism.[22-24] Furthermore, the vaso-active peptides, angiotensin II, vasopressin and endothelin, also stimulate cardiac PI metabolism.[25,26]

Several recent discoveries indicate that the PI pathway might be of particular importance in atrial tissue: (*i*) activation of the PI pathway has been suggested as a mediator of ANP release by catecholamines and cholinergic agents;[27,28] (*ii*) dilatation of the right atrium causes stimulation of PI turnover;[29] (*iii*) Ins (1,4,5)P_3 releases intracellular Ca^{2+} in permeabilised chick atria;[30] (*iv*) norepinephrine-induced stimulation of PI turnover is significantly higher in the atria than in the ventricles;[23] (*v*) the potent vasoconstrictor peptide, endothelin, releases ANP from isolated atria[17] and also causes a significant increase in PI turnover in the atria;[26] (*vi*) the incorporation rate of [^{3}H]-inositol into the inositol phosphates is two- to three-fold higher in atria than in ventricles;[31] and (*vii*) preliminary results from our own labo-

EDITORIAL/VAN DIE REDAKSIE

ratory indicate Ins(1,4,5)P_3 tissue levels as well as receptor density to be higher in the atria than in ventricles.[31]

The association between the high metabolic activity of the PI pathway in the atria, its role in the regulation of Ca^{2+} homeostasis and ANP release, and its regulation by endothelin and angiotensin II suggest a possible complex interaction between the PI pathway and the endocrine activities of the heart.

Another peculiarity which further demonstrates the uniqueness of atrial tissue is the recent demonstration of specific and high-affinity binding areas for relaxin (a reproduction hormone) in atrial tissue.[32] However, the source of relaxin for atrial binding as well as its effects on the cardiovascular system remains to be elucidated.

Not only do the atria differ from the ventricles, but a clear difference between the two atria has also been identified. Thus the following biochemical and physiological activities have been shown to be higher in the *right* atrium: (*i*) tissue levels of angiotensin I and II,[9] ANP mRNA and ANP,[33] acetylcholine[34] and neuropeptide Y;[35] (*ii*) stimulation of the PI pathway by endothelin,[26] noradrenaline[23] and stretch;[29] and (*iii*) eicosanoid synthesis.[36]

In view of the crucial position of the right atrium as the first recipient of venous blood from the peripheral and coronary circulations, these findings seem to suggest a unique role as 'biochemical pacemaker' of the cardiovascular system in tandem with its electrophysiological pacemaking activities.

The rapid expansion of knowledge in this very complex field of atrial cardiology at present is not only leading towards the formulation of novel hypotheses regarding the true functions of the endocrine heart, but it may eventually also lead to the design and development of novel and more rational therapeutic approaches to circulatory disorders.

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1. Kisch B. A significant microscopic difference between the atria and the ventricles of the mammalian heart. *Exp Med Surg* 1963; **21:** 193-221.
2. Koch-Wesser J, Blinks JR. The influence of the interval between beats on myocardial contractility. *Pharmacol Rev* 1963; **15:** 601-652.
3. Davies F, Francis ET, Stoner HB. The distribution of nucleotide, phosphocreatine and glycogen in the heart. *J Physiol* 1947; **106:** 154-166.
4. McDonald TF, Macleod DP. Anoxic atrial and ventricular muscle electrical activity, cell potassium, and metabolism: a comparative study. *J Mol Cell Cardiol* 1973; **5:** 149-159.
5. Lindpainter K, Ganten D. The cardiac renin-angiotensin system. *Circ Res* 1991; **63:** 905-921.
6. Campbell DJ, Habener JF. The angiotensin gene is expressed and differentially regulated in multiple tissues of the rat. *J Clin Invest* 1986; **78:** 31-39.
7. Lindpainter K, Jin M, Niedermeyer N, Wilhelm MJ, Ganten D. Cardiac angiotensinogen and its local activation in the isolated perfused beating heart. *Circ Res* 1990; **67:** 564-573.
8. Fabris B, Jackson B, Cubela R, Mendelsohn FAO, Johnston CI. Angiotensin converting enzyme in the rat heart: studies of its inhibition in vitro and ex vivo. *Clin Exp Pharmacol Physiol* 1989; **16:** 309-313.
9. Lindpainter K, Wilhelm MJ, Jin M, Unger T, Lang RE, Schoelkens BA, *et al.* Tissue renin-angiotensin systems: focus on the heart. *J Hypertens* 1987; **5** (suppl 2): 33-38.
10. Baker KM, Singer HA. Identification and characterization of guinea pig angiotensin II ventricular and atrial receptors: coupling to inositol phosphate production. *Circ Res* 1988; **62:** 896-904.
11. Ruskoaho H, Kinnunen P, Taskinen T, Vuolteenaho O, Leppaltuoto J, Takala TES. Regulation of ventricular atrial natriuretic peptide release in hypertrophied rat myocardium. Effects of exercise. *Circulation* 1989; **80:** 390-400.
12. Opie LH. *The Heart.* 2nd ed. New York: Raven Press, 1991: 417-419.
13. Dietz JR. Control of atrial natriuretic factor release from a rat heart-lung preparation. *Am J Physiol* 1987; **252:** R498-R502.
14. Bilder GE, Siegl PKS, Schofield TL, Friedman PA. Chronotropic stimulation: a primary effector for release of atrial natriuretic factor. *Circ Res* 1989; **64:** 799-805.
15. Schiebinger RJ, Linden J. The influence of resting tension on immunoreactive atrial natriuretic peptide secretion by rat atria superfused in vitro. *Circ Res* 1986; **59:** 105-109.
16. Fukada Y, Hirata Y, Taketani S, Kojima T, Oikawa S, Nakazato H, *et al.* Endothelin stimulates accumulations of cellular atrial natriuretic peptide and its messenger RNA in rat cardiocytes. *Biochem Biophys Res Commun* 1989; **164:** 1431-1436.
17. Hu JR, Berninger UG, Lang RE. Endothelin stimulates atrial natriuretic peptide (ANP) release from rat atria. *Eur J Pharmacol* 1988; **158:** 177-178.
18. Ruskoaho H, Vakkuri O, Arjamaa O, *et al.* Pressor hormones regulate atrial-stretch-induced release of atrial natriuretic peptide in the pithed rat. *Circ Res* 1989; **64:** 104-111.
19. Ferrari R, Anand I. Neurohumoral changes in untreated heart failure. *Cardiovasc Drugs Ther* 1989; **3:** 979-986.
20. Giles TD. Defining the role of atrial natriuretic factor in health and disease. *J Am Coll Cardiol* 1990; **15:** 1331-1333.
21. Berridge MJ. Inositol trisphosphate and diacylglycerol: two interacting second messengers. *Ann Rev Biochem* 1987; **56:** 159-193.
22. Brown JH, Buxton IL, Brunton LL. α_1-Adrenergic and muscarinic cholinergic stimulation of phosphoinositide hydrolysis in adult rat cardiomyocytes. *Circ Res* 1985; **57:** 532-537.
23. Woodcock EA, Schmauk White LB, Smith AI, McLeod JK. Stimulation of phosphatidylinositol metabolism in the isolated, perfused rat heart. *Circ Res* 1987; **61:** 625-631.
24. Mouton R, Huisamen B, Lochner A. Increased myocardial inositol trisphosphate levels during alpha$_1$-adrenergic stimulation and reperfusion of ischaemic rat heart. *J Mol Cell Cardiol* 1991; **23:** 841-850.
25. Leung E, Johnston CI, Woodcock EA. Stimulation of phosphatidylnositol metabolism in atrial and ventricular myocytes. *Life Sci* 1986; **39:** 2215-2220.
26. Kuraja IJ, Woodcock EA. Endothelin stimulates inositol phosphate accumulation in rat right and left atria: a comparison with noradrenaline. *Clin Exp Pharm Phys* 1990; **17:** 275-280.
27. Sonnenberg H, Veress AT. Cellular mechanisms of release of atrial natriuretic factor. *Biochem Biophys Res Commun* 1984; **124:** 443-449.
28. Currie MG, Newman WH. Evidence for alpha$_1$-adrenergic receptor regulation of atriopeptin release from the isolated rat heart. *Biochem Biophys Res Commun* 1986; **137:** 94-199.
29. Von Harsdorf R, Lang RE, Fullerton M, Woodcock EA. Myocardial stretch stimulates phosphatidylinositol turnover. *Circ Res* 1989; **65:** 494-501.
30. Vites AM, Pappano A. Inositol 1,4,5-trisphosphate releases intracellular Ca^{2+} in permeabilized chick atria. *Am J Physiol* 1990; **258:** H1745-H1752.
31. Mouton R, Genade S, Huisamen B, Lochner A. The effect of ischaemia-reperfusion on $InsP_3$ levels in cardiac atria and ventricles — a comparative study. *J Mol Cell Cardiol* 1992; **24** (suppl 1): S142.
32. Osheroff PL, Cronin MJ, Lofgren JA. Relaxin binding in the rat atrium. *Proc Natl Acad Sci* 1992; **89:** 2384-2388.
33. Arai H, Nakao K, Saito Y, Morii N, Sugawara A, Yamada T, *et al.* Simultaneous measurement of atrial natriuretic polypeptide (ANP) messenger RNA and ANP in rat heart — evidence for a preferentially increased synthesis and secretion of ANP in left atrium of spontaneously hypertensive rats (SHR). *Biochem Biophys Res Commun* 1987; **148:** 239-245.
34. Nomura A, Yasuda H, Takechi S, Matsuo H, Maruyama Y. Cardiac acetylcholine concentration in the rat. *Life Sci* 1990; **47:** 135-139.
35. Han C, Wang XA, Fiscus RR, Gu JA, McDonald JK. Changes in cardiac neuropeptide Y after experimental myocardial infarction in rat. *Neurosci Lett* 1989; **104:** 141-146.
36. Mentz P, Pawelski KE, Giessler C, Mest HJ, Mannes F, Rotzoll S. Myocardial biosynthesis of prostacyclin and the influence of cardiac loading and drugs. *Biomed Biochim Acta* 1988; **47:** 244-247.