MEETING REPORT

The biennial scientific meeting of the International Society of Hypertension is rightly regarded as the premier international hypertension congress. It attracts researchers in hypertension at all levels, ranging from basic molecular biology and cell biochemistry up to and including epidemiology. This year, the congress took place in an idyllic setting, in a functionally near-perfect congress hall in the middle of beautiful Takaragaike park in Kyoto. The organization, by Professors Kaneko, Omae, and their colleagues, was outstanding.

A total of 1,448 abstracts was received from 45 countries. 370 (26%) papers were accepted for the main meeting either as oral (60) or poster (310) presentations. In addition there were 24 satellite symposia which allowed some additional 350 abstracts to be accepted for presentation.

A selection from this wealth of material can only be somewhat arbitrary. I believe, however, that two of the clearly defined research areas in which significant advances were reported were, first, factors affecting the rate of growth of vascular smooth muscle cells and cardiac myocytes, and second, new cell peptides concerned with vascular contractility.

Vascular and Cardiac Growth Factors

These factors obviously have great relevance to the generation of atherosclerosis and myocardial hypertrophy in hypertension. Hamet et al. [1], from the Clinical Research Institute of Montreal, reminded the congress that vascular smooth muscle cell hyperplasia has been demonstrated in the vessel wall in hypertension and may be one of the primary factors in its pathogenesis. Vascular smooth muscle cells derived from spontaneously hypertensive rats (SHR) grow at rates greater than Wistar Kyoto (WKY) controls, even in cell culture. The proliferation response to calf serum or separately administered platelet-derived growth factor (PDGF) or epidermal growth factor (EGF) was significantly higher in the SHR-derived cells than in WKY. A similar finding was reported by Resink and colleagues [2] from Basel, Switzerland, namely, that EGF induced vascular smooth muscle cell proliferation is greater in SHR than WKY. They found an increased receptor density for EGF in SHR than in WKY. SHR-derived vascular smooth muscle cells also exhibited greater functional responsiveness to EGF as evidenced by amplifications of both S6 kinase and phosphoinositide turnover activation responses.

Naftilan and colleagues [3, 4] from Boston, addressed the interesting observation that angiotensin II causes hypertrophy in cultured aortic smooth muscle cells, and found that angiotensin II activates mRNA for a number of proto-oncogenes and PDGF. On the subject of angiotensin and vascular smooth muscle, it is now known that all of the components of the renin-angiotensin system are present in vascular smooth muscle. This includes renin, angiotensin I and II, and renin substrate. Aortic angiotensinogen mRNA levels are seven times higher in WKY than in SHR, and also are stimulated, in WKY but not in SHR, by a low-sodium diet, suggesting an altered vascular angiotensinogen gene in SHR which may have important physiologic implications. Darby et al. [5] from Paris, Montpellier, and Lausanne, showed that angiotensin II stimulated DNA synthesis during the first 6 hours of treatment of a hepatoma cell line Hep G2 as measured by $^3$H-thymidine uptake. They suggested that the Hep G2 cells possessed specific angiotensin II receptors, and that angiotensin II has a mitogenic effect in these cells. Morton and colleagues [6], from Glasgow, showed that angiotensin II increased vascular smooth muscle cell number in a dose-dependent manner compared to controls, confirming that angiotensin II is a VSM mitogen, and suggested that this may operate via the Na$^+$/H$^+$ antiport of the cell membrane.

Adams and colleagues [7] from Prahran, Australia, followed the magnitude and progression rate of cardiac and vascular hypertrophy in relation to the activity of the sympathetic nervous system in 4-to 50-
week-old SHR and WKY rats. The degree of relative vascular hypertrophy was hemodynamically assessed from the pressure elevation at maximum constriction in paired SHR WKY hindlimb vascular preparations. Cardiac hypertrophy was determined from left ventricle to body weight ratio, and an index of sympathetic activity was obtained by measuring noradrenaline turnover using α-methyl-p-tyrosine. Vascular hypertrophy occurred very early in the SHR, preceding the development of hypertension, whereas cardiac hypertrophy was present to a small extent in young rats but subsequently developed with increasing blood pressure. There seemed to be a good correlation between cardiac hypertrophy and cardiac sympathetic activity. Adams et al. concluded that there is “primary” hypertrophy of blood vessels compared with “secondary” changes in the heart. The increase in cardiac sympathetic activity may contribute to the development of left ventricular hypertrophy.

What are the effects of antihypertensive treatment on vascular and ventricular structural changes? This question was addressed by Agabiti-Rosei et al. [8] from Brescia, Italy, who studied 14 patients with hypertension and measured blood pressure, left ventricular systolic function, and mass index by echocardiography and basal and postischemic maximal forearm blood flow by strain gauge venous occlusion plethysmography. Patients were treated with various combinations of captopril, hydrochlorothiazide, nitrendipine, and atenolol and were followed for 12 months, during which time left ventricular mass index was normalized before complete regression of arterial structural changes occurred in the forearm.

New Cell Peptides Concerned with Vascular Contractility

Takahashi and associates [9], from Ehime, Japan described a novel calcium-and calmodulin-binding troponin T-like protein named calponin, which has been purified from bovine aorta smooth muscle. The immunoreactive form of this protein with Mr34000 was localized on the microfilament bundles. Immunoelectron microscopy showed that on the thin filaments there were calponin bands with about 38 nm periodicity. The authors suggest that a calponin molecule, in association with a tropomyosin and seven actin monomers on one actin strand, may form a regulatory unit in vascular smooth muscle thin filaments.

Another novel peptide described was endothelin, by Yanagisawa, Kurihara et al. [10, 11] from Tsukuba, Ibaraki, and Tokyo, Japan. Since the discovery in 1980 of endothelium-dependent vasodilatation by Furchgott and Zawadzki [12], vascular endothelium has been recognized as an important functional unit involved in the regulation of vascular smooth muscle tone. Yanagisawa and colleagues have described a potent protease-sensitive vasoconstrictor activity in the culture supernatant of vascular endothelial cells. Endothelin, a 21-residue peptide with two intrachain disulfide bonds, is the most potent vasoconstrictor peptide known to date. It is produced de novo in epithelial cells from a 203-residue prepropeptide.

The vasoconstrictor effect of endothelin on porcine coronary artery was resistant to blockade by α-adrenergic, cholinergic, histaminergic, and serotoninergic agents, and to cyclo-oxygenase and lipo-oxygenase inhibitors. Responses were inhibited by nicardipine and appeared to be absolutely dependent on the extra-cellular calcium concentration. To examine whether the production of endothelin by endothelial cells was regulated in response to vasoactive agents, porcine aortic endothelial cells were cultured in the presence of adrenalin, thrombin, or the calcium ionophore A23187, and the expression of preproendothelin mRNA was increased severalfold within 1 hour. These findings all suggest that there is a novel endothelium-mediated regulation in the mammalian cardiovascular system, which is vasoconstrictor, may act via changes in calcium flux, and the production of which is stimulated by a number of other vasoactive agents.

References

2. Resink TJ, Scott-Burden T, Buhler FR. Increased responsiveness to epidermal growth factor in cultured vascular smooth muscle cells from spontaneously hypertensive rats. Ibid. 1005.