ABSTRACTS

Abstracts for Invited Lectures:

IL1.

Endothelial Dysfunction in Hypertension

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The endothelial cells cause relaxations (dilatations) or contractions (constrictions) of the underlying vascular smooth muscle cells by releasing diffusible vasoactive substances. The endothelium-derived relaxing factors (EDRF) include nitric oxide (NO) endothelium-derived hyperpolarizing factor (EDHF) and prostacyclin. The release of EDRF from the endothelium can be mediated by both pertussis toxin-sensitive ($alpha_2$-adrenergic activation, serotonin, aggregating platelets, leukotrienes) and insensitive (adenosine diphosphate, bradykinin) G-proteins. The ability of the endothelial cell to release relaxing factors is reduced in blood vessels of animals and patients with hypertension. This favors the occurrence of vasospasm, thrombosis and cellular growth. In addition to relaxing factors, the endothelial cells can produce contracting-substances (endothelium-derived contracting factors; EDCFs) which include endoperoxides, prostacyclin and thromboxane A_2. These prostanoids cause contraction of the underlying vascular smooth muscle by activating TP-receptors. The propensity to release EDCFs is augmented in hypertension. The switch from a normally predominant release of EDRFs to that of EDCFs may play a crucial role in vascular hyperreactivity seen in hypertension and favors the occurrence of atherosclerosis.

IL2.

Research on Novel Targets Regulating Cardiac Ischemic Arrhythmias

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Aim: This study was designed to investigate whether MicroRNA (miRNA) is involved in cardiac ischemic arrhythmias, in addition to its role in regulating development.
Methods: Rat model of myocardial infarction was performed. The human tissues were from six rejected hearts of healthy persons and from seven explanted hearts of CAD individuals. MiR-1 levels were measured using miRNA Detection Kit. Intramuscular injections were made in approximately 10 sites before coronary artery occlusion. The K^+ current I_{K1} was measured using whole-cell patch-clamp. Conduction velocity was measured on the ventricular epicardial surface in perfused hearts.
Results: MiR-1 is overexpressed in individuals with coronary artery disease, and that when overexpressed in normal or infarcted rat hearts, it exacerbates arrhythmogenesis. Elimination of miR-1 by an antisense inhibitor in infarcted rat hearts relieved arrhythmogenesis. MiR-1 overexpression slowed conduction and depolarized the cytoplasmic membrane by post-transcriptionally repressing KCNJ2 (which encodes the K^+ channel subunit Kir2.1) and GJA1 (which encodes connexin 43), and this likely accounts at least in part for its arrhythmogenic potential.
Conclusion: MiR-1 may have important pathophysiological functions in the heart, and is a potential antiarrhythmic target.

IL3.

Cyclooxygenase-dependent Endothelial Dysfunction in Renovascular Hypertension

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The normal vascular function is maintained by the balance between endothelium-derived relaxing factors (EDRF) and constricting factors (EDCF), which are involved in the regulation of vascular tone. Under hypertensive conditions, the balance tilts towards EDCF, which contributes to the increased vascular contraction and blood pressure. Animal models of renovascular hypertension such as two-kidney, two-clip or two-kidney, one-clip rats show the impaired endothelial cell function caused by unfavorable changes in both vascular reactivity and structure of blood vessels. However, it is unknown whether endothelial dysfunction in renovascular hypertension is associated with the increased expression and function of EDCFs. The present study aimed to investigate mechanisms underlying impaired endothelium-dependent relaxation in the isolated intrarenal arteries from experimentally induced renovascular hypertensive rats (RHR). Acetylcholine causes less relaxations in RHR arteries and triggers endothelium-dependent contractions only in N^G-nitro-L-arginine methyl ester-treated rings with endothelium. The endothelium-dependent contractions are abolished in rings treated with indomethacin (cyclooxygenase inhibitor) and by NS 398, DUP 697 or celecoxib (COX-2 inhibitors). The thromboxane prostanoid (TP) receptor antagonist, S18886 also eliminates the contraction to acetylcholine. By contrast, the contractions are unaffected by cycloheximide (protein synthesis inhibitor). The present results demonstrate that the endothelium-dependent contractions in RHR renal arteries are mediated by COX-2-dependent metabolic products of arachidonic acid, which act as putative EDCFs. Chronic treatment with celecoxib for 5 weeks ameliorates endothelial dysfunction and attenuates endothelium-dependent contraction. The novel findings of the present study support a critical role of COX-2 renovascular hypertension-associated endothelial dysfunction and COX-2 could be am important target enzyme for therapeutic intervention in renovascular hypertension.

ABSTRACTS

Abstracts for Invited Lectures:

IL4.

The Role of the Renin Angiotensin System in Blood Pressure Regulation and Hypertension

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The renin angiotensin system (RAS) through the generation of angiotensin II (AII) with potent vasoconstrictor and sodium retention properties controls the characteristics of the pressure- natriuresis curve and is therefore of paramount importance in BP regulation and the development of hypertension (HTA). As a consequence one of the most successful approaches of the treatment of HTA relied on the blockade of the RAS. This is currently achieved using angiotensin-converting enzyme (ACE) inhibitors or AII receptors (AT1R) blockade. More recently, specific inhibitors of renin have been tested alone or in combination with thiazides and showed similar efficacy as other RAS blockers. Interestingly, besides BP decrease, RAS blockade seems to have additional properties such as slowing the development of type 2 diabetes and preventing the kidneys from nephroangiosclerosis. In that respect, we checked the hypothesis that low, non antihypertensive doses of ACE inhibitors may exhibit significant nephroprotective properties. This was performed in a model of genetically hypertensive rats that we developed in Lyon (LH rats). These rats associate, in a quite specific fashion, spontaneous hypertension with several features which evoke a metabolic syndrome, such as overweight, hyperlipidemia, elevated insulin/glucose ratio and marked proteinuria. Groups of LH rats were chronically treated with orally given perindopril – an ACE inhibitor – at doses ranging from 0.01 to 0.4 mg/kg/24h. It was observed that BP was significantly decreased only by the 0.4 mg/kg/24 h dose, while the urinary excretion of proteins was reduced by the lower non antihypertensive ones. In conclusion, we can postulate that chronic treatment with low doses of perindopril may be useful to attenuate the evolution of early diagnosed renal alterations.

IL5.

Changing the Anti-Hypertensive Drug Treatment – Implicatins from International Hypertension Guidelines

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Hypertension, one of the commonest diagnoses in the clinic, contributes substantially to the morbidity and mortality of cardiovascular disease (CVD). However, despite well recognized as an important risk factor of CVD, management of hypertension remained unsatisfactory, since less than 30 percent of hypertensive patients were well treated. In recent years, there were at least 4 important guidelines for treatment of hypertension published: (1) 2003 JNC 7 guideline; (2) 2003 ESC/ESH guideline; (3) 2003 WHO/ISH guideline; (4) 2004-BHS IV guideline. And the most updated ESC/ESH hypertension guideline was just published in 2007. In this presentation, I will address the highlight of the current international guidelines and give a brief summary. Furthermore, I will also introduce the current prescription patterns and factors influencing the switch in the use of anti-hypertensive medications in Taiwan.

IL6.

New Trends in the Management of Arterial Hypertension

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The management of arterial hypertension has been for years, a continuous challenge for every physician. All data published over the years have shown that treatment clearly is capable of improving prognosis and correcting organ damage caused by elevated blood pressure. However, more and more data are available indicating that control of blood pressure still remains under the level of what actual medical care could provide us with. The newly published guidelines (2007) certainly will help in getting better results. One of the striking issues in these guidelines is the concept that hypertension no longer should be seen as an alone standing entity but rather as a part of total cardiovascular risk. Accompanying risk factors and other existing cardiovascular abnormalities can render the risk linked to hypertension highly different. For example, mild blood pressure elevation can become a high risk condition if other risk factors (lipids, weight...) are present. Vice versa, a high blood pressure figure can become much lower risk when other risk factors are absent. Therefore, BP elevation should be seen in its actual context and not only as a numerical value. Such new ideas will be further discussed several clinical cases at hand.