INNOVATIVE CONCEPTS OF HYPERTENSION TO UNDERSTAND AND MANAGE THE DISEASE

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Studies on Mendelian hypertension have provided great insight into mechanisms causing hypertension. Mineralocorticoid synthesis and degradation, the mineralocorticoid receptor, sodium channel resorptive mechanisms, and regulation of the thiazide-sensitive sodium-chloride cotransporter have been shown to cause hypertension. Aberrant regulation of peripheral vascular resistance and circulatory regulation have not yet been proved but have been strongly implicated in Mendelian hypertension with brachydactyly. Hypertension as a complex genetic trait has proved more difficult because many genes are involved and the genes have much smaller effects. Association studies, linkage analyses, single nucleotide polymorphism analyses, synteny in animal models, and gene expression studies are the current tools and steady progress is being made.

Tissue Renin Angiotensin Systems 19
Richard N. Re

The renin-angiotensin-aldosterone system (RAAS) is a well-established regulator of intravascular volume and blood pressure. An increasing body of evidence indicates that various components of the renin-angiotensin system (RAS) are either differentially taken up into tissues from the circulation or independently synthesized in tissues, with the result that the tissue concentrations of the effector hormone angiotensin can be locally determined. Evidence also has been developed that renin and prorenin can function in a hormone-like fashion, binding to specific receptors and generating second-messenger cascades. Finally, the components of the RAS seem to be capable of functioning in an intracellular, or intracrine, mode. Collectively, these observations suggest an expanded view of the role of the RAAS in health and disease, and point to an important role for tissue RASs.
Significance of Recently Identified Peptides in Hypertension: Endothelin, Natriuretic Peptides, Adrenomedullin, Leptin
Carmine Savoia and Ernesto L. Schiffrin

Arterial hypertension is one of the major risk factors in cardiovascular and renal disease. Advances in the study of pathophysiologic mechanisms and the relationship between several regulatory systems provide the basis for development of more selective therapeutic strategies. The increasing understanding of the role played by endothelins, natriuretic peptides, adrenomedullin, and leptin opens new frontiers in the care of hypertension and its complications, coronary artery disease, and heart failure and other forms of cardiovascular disease.

Insulin and Insulin Resistance: Impact on Blood Pressure and Cardiovascular Disease
James R. Sowers and Edward D. Frohlich

Insulin (INS) resistance is an integral component of the cardiometabolic syndrome, which often progresses to type 2 diabetes and cardiovascular disease (CVD) events. Hyperinsulinemia, an important component of the cardiometabolic syndrome, may predispose to the development of hypertension, another important part of this syndrome. Hyperinsulinemia may directly contribute to elevated blood pressure by enhancing sympathetic nervous system activity and promoting renal sodium retention. INS may also indirectly increase blood pressure by decreasing the signaling processes that are important for vascular relaxation. Further, an overexpression of the tissue renin-angiotensin system seems to contribute to impaired INS use in skeletal muscle and fat tissue and diminished vasorelaxation. Therapeutic strategies that improve INS sensitivity may impede the progression of impaired INS sensitivity to that of clinical diabetes, and reduce blood pressure, renal disease progression, and CVD events.

Fibrosis in Hypertensive Heart Disease: Role of the Renin-Angiotensin-Aldosterone System
Arantxa González, Begoña López, and Javier Díez

Myocardial fibrosis is critically involved in the transition from adaptive left ventricular hypertrophy to heart failure in arterial hypertension. A growing body of evidence suggests that angiotensin II is actively involved in alterations of fibrillar collagen metabolism leading to fibrosis in hypertensive heart disease. Strategies aimed to counteract the profibrotic actions of the peptide may provide a beneficial effect in terms of heart failure prevention in hypertensive patients.

Coronary Flow Reserve Measurements in Hypertension
Malte Kelm and Bodo E. Strauer

Arterial hypertension can provoke a reduction in coronary flow reserve through several mechanisms that are not mutually exclusive.
The diagnostic management should include exploring these different targets with different diagnostic markers. In clinical practice one should keep in mind that assessing global cardiovascular risk of hypertensive patients into low, medium, high, and very high class is the primary goal. This article discusses variables of coronary flow regulation as far as they seem crucial for the understanding of diagnostic procedures to assess coronary flow reserve in arterial hypertension.

Cardiac Remodeling in Systemic Hypertension
Satish Kenchaiah and Marc A. Pfeffer

Experimental and clinical studies provide evidence that hypertension is causally related to adverse cardiac structural changes. These changes are induced by both hemodynamic and nonhemodynamic factors. There is accumulating evidence from several small and large clinical trials that various classes of antihypertensive therapy prevent and regress left ventricular hypertrophy and myocardial fibrosis. In patients with hypertensive heart disease, the components of therapy must comprise optimization of blood pressure and regression of left ventricular hypertrophy. Future targets of therapy in hypertensive heart disease may include regression of myocardial fibrosis, normalization of left atrium size, and improvement in left ventricle diastolic function.

Renal Function in the Patient with Hypertension
Norman Kenneth Hollenberg

The kidney is both a cause of hypertension and a major target organ for damage in patients with hypertension. In this article major emphasis is given to the diagnosis of renal disease as a cause of hypertension and the management of selected complications of hypertension involving the kidney.

What Can We Expect from New Guidelines?
Norman M. Kaplan

New guidelines for the treatment of hypertension are being published, starting with the seventh report of the US Joint National Committee. These guidelines are certain to address the major developments that have been presented over the past few years. These include the risks of any level of increased blood pressure, either alone or in concert with other known risk factors; the value of out-of-office blood pressure measurements; the preventive potential of lifestyle changes; the results of multiple prospective comparative trials, which have largely negated the quest for the best initial choice of therapy; and the need to increase adherence to enough therapy to reach the appropriate goal for each patient.
Evolving Role of Calcium Antagonists in the Management of Hypertension
Murray Epstein and Vito M. Campese

Since their introduction more than 30 years ago, calcium antagonists have emerged as one of the most attractive and widely used classes of antihypertensive agent. Recent studies have demonstrated that calcium antagonists have beneficial effects in coronary artery disease, which may be attributed to distinct antiatherosclerotic properties related to its strong lyophilicity. Furthermore, calcium antagonists potentially have beneficial effects that are related to their noncalcium-related pleiotropic actions. This article focuses on a number of key issues that are pivotal to this discussion.

Continued Importance of Diuretics and β-Adrenergic Blockers in the Management of Hypertension
Marvin Moser and John Setaro

Diuretics and β-adrenergic blockers have been shown to be effective and well-tolerated antihypertensive medications. Numerous large randomized clinical trials have demonstrated that the use of these compounds results in a reduction in morbidity and mortality in hypertensive patients. Despite some questions that continue to be raised about metabolic changes that may occur with these medications, newer trials have reaffirmed their safety and benefits in the management of high blood pressure, both as monotherapy and as part of combination therapy in more complex or difficult management situations. In the current era, lower treatment thresholds and stricter blood pressure goals will ensure that diuretics and β-blockers continue to have a fundamental role in hypertension management.

What have We Learned from the Current Trials?
Kevin C. Abbott and George L. Bakris

The twenty-first century has opened with an explosion of landmark randomized clinical trials assessing the impact of therapeutic agents on outcomes in hypertensive patients. The trials discussed in this article are in the opinion of the authors the most significant studies of the new century in several categories: (1) assessment of the impact of agents on incident cardiovascular disease in high-risk patients in the general population (ie, in patients at high risk for but not exclusively those with known prevalent disease); (2) progression of renal disease in patients with type II diabetes; and (3) outcomes in high-risk ethnic subgroups (ie, African Americans). Agents featured include diuretics versus angiotensin-converting enzyme inhibitors or calcium channel blockers for de novo events, angiotensin receptor blockers for progression of diabetic renal disease, and angiotensin-converting enzyme inhibitors versus calcium channel blockers in African Americans with hypertensive nephropathy.
End points from hypertensive disease, stroke, coronary heart disease, and hypertensive emergencies can be markedly reduced. However, cardiac failure and end-stage renal disease, two exceedingly common end points from long-standing hypertension, remain as major disabilities and causes of death. Present day therapy now can effectively reverse these costly (economically and by human suffering) complications, and recent experimental studies suggest that, when used early enough, these newer pharmacologic agents may even prevent their occurrences and consequences. The very practical lesson from these experiences is that early detection and treatment of hypertension, effective control of arterial pressure, and the suppression of the underlying disease mechanisms markedly reduce the now increasing prevalence of both cardiac and renal failure.

Despite progress in recent years in prevention, detection, and treatment of high blood pressure, hypertension remains an important public health challenge. Primary prevention of hypertension provides an avenue to interrupt and prevent the continuing costly cycle of managing this disease and its complications. This article reviews the new recommendation for classification of hypertension, updated information on the incidence of hypertension, and an overview of lifestyle interventions for primary prevention of this chronic disease.