Blood Pressure and Arterial Wall Mechanics in Cardiovascular Diseases

Michel E. Safar • Michael F. O'Rourke
Edward D. Frohlich
Editors

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Introduction

Three colleagues whose background in medicine arose from their similar interests in cardiovascular research, although they never worked at the same institution, conceived the concept of this textbook. Further, even more unique, they lived throughout their professional careers in three disparate continents and countries: France, Australia, and the United States. Each of them conducted their clinical investigation in cardiovascular medicine. Initially, Professors Safar and Frohlich were interested primarily in a developing area concerned with the hemodynamics of hypertension. They first met in 1962 when Ed Frohlich was on staff of the Research Division of the Cleveland Clinic in Ohio. Michel Safar visited the Cleveland group at that time to exchange thoughts on a now-forgotten topic concerning the underlying mechanisms of "labile" hypertension. Michel was on the Faculty of Medicine at the Broussais Hospital in Paris. They both shared similar thinking about one aspect in the pathogenesis of hypertensive disease: an initial increased cardiac output, which was produced by total body venoconstriction resulting in increased venous return associated with an "inappropriately normal" total peripheral resistance. Ed continued his work with the role of the heart in hypertension and the underlying mechanisms which may explain its increased risk for morbidity and mortality associated with left ventricular hypertrophy. This, of course, stimulated further interest in left ventricular hypertrophy and its interaction with antihypertensive therapy and its impact on cardiac risk. Other factors confounded that risk including the effects of long-term dietary sodium excess on the cardiovascular and renal inter-relationships. Thus, Michel and Ed continued to remain closely related personally and academically in their clinical investigative interests.

During these years, Michel Safar focused his efforts on the pathophysiological mechanisms responsible for the role of the large arteries in hypertension and its consequences in patients with essential hypertension. He and his team of investigators made their major impact on the development of a new area of clinical research responsible for the increasing interest in systolic hypertension in the elderly and the field of "stiffness" of the large arteries. This, of course, brought Michel Safar into the third relationship with Michael O'Rourke whose fundamental research on large arteries in Australia involved work with a physiological pioneer, Michael Taylor, on comparative physiology and computer modeling of arterial networks. This led to clinical studies on ventricular/vascular interactions, intra-aortic balloon counterpulsation, cardiac transplantation and mechanical heart assist devices. His

studies promoted interests in the aging process, which develops slowly from early adulthood and involves stiffening and dilation of the aortic wall. These hemodynamic interests led to the collaborative efforts of Michael and Michel in the fields of pulsatile arterial parameters and aortic rigidity. They now consider the possibility that small vessel disease in the brain, causing dementia, is another consequence of aortic stiffening and early wave reflection, which may be prevented or delayed by measures which reduce effects of aortic stiffening. The immediate result of their relationship was Michel's establishment of a regular series of international workshops in Paris on this new area of research resulting in a remarkably increased pursuit of scholarly activity in both the fundamental and clinical investigative aspects in this area.

Contemporaneously, during these years, Ed Frohlich assumed editorial responsibility for the American Heart Association's journal *Hypertension*, and was delighted to join "forces" with Michel and Michael to publish the periodic proceedings of the workshop in that journal. This is the story of our personal collaborations and continuing research, based on long-standing friendship and the influence of Michel Safar in the three of us joining together our mutual interest. This now has resulted in publication of this volume involving similarly committed colleagues from the world-wide academic community. Indeed, it explains our joint conception of the title and content of this work of long-standing friends and academic co-workers and the large co-authorship of its contributors.

Basic Concepts of the Book

Our most common and classical knowledge on blood pressure and hypertension has been primarily influenced by three key-points. First, the hemodynamic mechanisms of hypertension have been primarily associated with an increase in total peripheral resistance, pointing to a major contribution of the role of small arteries. Second, the respective contributions of the heart, vessels, and kidneys involve major interactions affecting particularly the renin-angiotensin-aldosterone system. Finally, drug treatment modifies substantially cardiovascular morbidity and mortality through the dominant role of blood pressure reduction.

The development of hypertension has considerably matured over the years for two reasons. Firstly, hypertension was no longer considered as a single homogeneous disease, but rather as a mosaic of interacting mechanisms associated with many other interrelated cardiovascular risk factors. Secondly, the primary objectives of study were no longer limited to a discussion of only control of arterial pressure. Primary objectives were focused on the means to diminish the underlying risk of cardiovascular stiffness and its consequences on morbidity and mortality. This goal was considered and pursued through numerous therapeutic trials designed to intervene on those pathophysiological mechanisms and the interrelationships that are involved with the development of injury and disease outcomes of these target organs.

Parts I and II of this book are related to blood pressure involving two different and complementary aspects: the role of arterial wall mechanics and

the underlying mechanisms of risk involving left ventricular hypertrophy and the role of dietary salt excess on the development of cardiac and renal failure through structural and functional impairment.

In Part I, the role of blood pressure in hypertension and cardiovascular diseases was no longer limited to the role of brachial artery BP measurements, frequently explored in the past but extended to the overall remaining portions of circulation, mainly located at the origin of the aorta. Thus, the concept of central blood pressure was introduced for those organs most related to the presence of cardiovascular risk (i.e., the heart, the brain and kidneys). Pressure measurements were associated to evaluations of flow, impedance to pulsatile flow, arterial stiffness, and other critical parameters as pulse amplification. An important aspect of Part I was the difference noted between steady and pulsatile arterial hemodynamics, two parameters highly and differently related to cardiovascular risk. As noted by Michael O'Rourke, most of these parameters refer to the approach suggested in the past by the principal pioneers of pulsatile arterial hemodynamics, McDonald, Womersley and Taylor. One important aspect is the concept of heart-vessel coupling and its consequences on cardiac structure and function.

Part II refers to the relation between blood pressure, the heart and kidneys. The role of vasoactive interactions are not primarily focused in this discussion but involve primarily the role of the underlying mechanisms of risk in left ventricular hypertrophy, heart failure, oxidative stress and nitric oxide, in relation with mainly dietary salt excess in the heart and kidney. Also investigated are details of the value of multicenter trials of pharmacological therapy on cardiovascular and renal function in hypertension and heart failure.

As a consequence, Part III summarizes the principal findings characterizing hypertension and cardiovascular diseases and the disturbed arterial wall mechanics and sodium balance within the cardiovascular system. Such modifications are studied successively in terms of brachial and central BP measurements and take into account both steady and pulsatile arterial hemodynamics, particularly the role of heart rate and pulse pressure amplification. In addition, organ damages are described extensively in Part III, evaluating the particular and specific roles of the heart, the brain and the kidneys.

Parts IV and V are focused on the different aspects of the clinical involvement necessary for evaluation of the cardiovascular system. First, the role of age, sex, metabolic and inflammatory factors is considered in detail. Second, a description of risk stratification is given, primarily affecting arterial stiffness and pulse pressure. The major role of ethnicity is particularly taken into account. Finally, among the various cardiovascular medications associated to treatment, the antihypertensive agents are mainly (but not exclusively) taken into account, studying in particular their impact on arterial stiffness and wave reflections. Each of these considerations are presented in terms of large vessels, based on the privilege of knowledge and not necessarily the evidence of recommendations frequently difficult to demonstrate.

Finally, this book has developed new conceptual approaches of hypertension and cardiovascular risk, taking into account three major points. First, hypertension should involve in its definition not only vascular resistance but also arterial stiffness, wave reflections and vascular rarefaction. Second,

hypertension does not reflect a simple linear relationship between blood pressure and target organ damage but is more complex – and not necessarily linearly affecting mechanical factors and different complications individually associated with the heart, brain and kidneys. Finally, the aim of treatment is no longer limited to a decrease in blood pressure but, rather, a reduction of cardiovascular risk and, in the long term, of residual risk. In this context, it is important that, whereas increased stiffness and early wave reflections caused by aging magnify cardiovascular risk (studies in Part I), the improvement of cardiac function by drug treatment (studies in Part II) may actually exacerbate the adverse effect of increased stiffness and wave reflections when these arterial parameters remain untreated, thereby further increasing cardiovascular risk. Again, it is evident that treatment must verify in the long term the major role of heart-vessel coupling. Modern concepts must include arterial properties as well as peripheral resistance and cardiac function.

Content of the Book

This book is published at the peak of a special evolution during which new concepts and knowledge on blood pressure and cardiovascular risk have been developed over recent years, which is associated with continued exciting aspects of disease and its treatment. First, studies have recognized that the duration of life has increased considerably in recent years promoting research into novel aspects of therapeutic interventions. Second, current investigations on the interactions between genetics and environment still remain difficult to delineate clearly in our patients. These difficulties explain the necessity to obtain numerous contributors participating in all five sections of this volume. Each section is composed of several chapters, each detailed by their respective authors. Importantly, their specific contributions and responsibility, and reflecting any changes by the co-editors. Due to the complexity of the subject, repetitions within this book have not been completely excluded from the studied description by the authors, other than in editorial context to facilitate reading.

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