A focused issue on nitric oxide (NO) is timely within a year of the award of the Nobel Prize for Biology and Medicine to the discovery of the fundamental roles of this simple gas in cardiovascular physiology and pathophysiology. At the time of the seminal report by Furchgott and Zawadzki of a labile endothelium-derived relaxing factor (EDRF) responsible for acetylcholine-induced vasodilation [1], it could not have been imagined that the substance responsible would turn out to have such a multiplicity of functions and effects, not just in the cardiovascular but also in many other systems. Our knowledge about NO has indeed advanced enormously since those early days.

This issue of Cardiovascular Research brings together several review articles covering many of these advances, as well as a selection of original articles that reflect continuing studies in the field. Sessa and colleagues [2] review the molecular biology of the NOSs, and the development of gene-modified mice as a powerful experimental tool for dissecting out the physiological and pathophysiological roles of NO. Andrew and Mayer [3] describe the enzymatic function of the NOSs, while Fleming and Busse [4] review the signal transduction of NOS activation. Leiper and Vallance [5] bring us up to date with the studies of endogenous inhibitors of the NOSs, compounds that may turn out to have important physiological and pathophysiological roles. The realisation that NO-dependent pathways may be modulated by angiotensin converting enzyme (ACE) has potentially far-reaching implications, not least with respect to therapeutic manipulations, and this area is reviewed by Linz and colleagues [6]. Kojda and Harrison [7] describe the fundamental role of the interactions between NO and reactive oxygen species in the genesis of endothelial dysfunction, and the involvement of these interactions in several pathological processes. Clinical investigation has progressed alongside the advances in basic science, and Drexler [8] reviews studies of coronary endothelial dysfunction in humans. The development of atherosclerosis is one of the most important long-term consequences of endothelial dysfunction. Jeremy and colleagues [9] review the current status of knowledge regarding the influence of NO in this process. In the last several years, it has been recognised that NO influences not only the vasculature but also the myocardium. Paulus and Shah [10] discuss the effects of NO on cardiac diastolic function in experimental preparations and in patients, while Balligand [11] reviews the regulation of myocardial b-adrenergic responsiveness by NO. Rakhit and Marber [12] present a review of quite recent data that implicate NO in myocardial ischaemic preconditioning. Perhaps the main therapeutic advance that has been developed as a direct result of research into NO is its use in inhaled form to treat various pulmonary disorders; this is reviewed by Hayward [13]. Other aspects of NO are covered by additional review articles, while the original articles encompass a broad range of topical areas, and illustrate the potential for advance in the field.

We hope that this issue will provide a state-of-the-art review of current knowledge, and will stimulate new research to address some of the important questions and controversies identified herein.

References


