HYPERTENSION IN THE GERIATRIC (over 65 yr) population is increasingly emerging as a significant health problem in this age group. It is estimated that over one-half of the population age 65 and over, a burgeoning number of the overall United States population, has hypertension, and this prevalence may be increasing (7). Of particular importance is the nature of the most common type of elevated geriatric blood pressure, an entity distinct to the aging population, characterized by an isolated increase in systolic pressure associated with a wide pulse pressure. This form of geriatric hypertension is associated with increased cardiovascular morbidity and mortality in the form of coronary artery disease, stroke, congestive heart failure, end-stage renal disease, and total cardiovascular deaths (4, 7). The pathophysiology of geriatric hypertension, manifest as systolic pressure elevation and widened pulse pressure, is attributed to a consequence of large artery “stiffness” (2, 4). This arterial stiffness imparts a functional abnormality in large arteries resulting in decreased compliance and produces a widened pulse pressure. Arterial stiffness and decreased compliance increases with age independently of mean arterial pressure or other traditional cardiovascular risk factors. Several studies demonstrate that treatment of geriatric systolic hypertension by reducing systolic pressure without altering diastolic pressure and with the resultant improvement in pulse pressure significantly lowers the risk of cardiovascular disease (2, 7).

Although the characteristics of the aging vasculature have been described in general structural and functional terms, there is a paucity of detailed information about the mechanisms producing geriatric arterial dysfunction. Gaining insight into the causes of geriatric arterial dysfunction is needed to shape therapies targeted for this specific age-related entity.

Although advanced aging may lead to structural changes intrinsic to the geriatric vessel, functionally impaired vasodilation may occur through reductions in the synthesis or bioavailability of factors such as nitric oxide (NO). Payne et al. (5) in this issue of the American Journal of Physiology—Regulatory, Integrative and Comparative Physiology have advanced our understanding of the interaction between oxidative stress and endothelial factors producing geriatric hypertension. Their results also raise many questions about the geriatric vasculature, its functional capabilities, the reasons for its age-related dysfunction, and the appropriate animal models to study this age-related pathophysiogy. Perhaps the most important contribution of this article is the establishment of a more realistic animal model to study geriatric hypertension. Most previous examinations of the impact of aging on vascular function have been performed in rats up to 12 mo of age (3). Payne et al. have set the standard for future geriatric hypertension studies by not only performing their experiments in spontaneously hypertensive rats (SHR) at 24 mo of age, but also initiating any treatment, such as antioxidant therapy, at 16 mo, thus giving the animal a full 8 mo of aging before analysis. The results of these studies confirm that the truly geriatric large vessel, such as the aorta, from a genetically hypertensive species, demonstrates impaired contractile capabilities. The studies further support a mechanistic scenario in which geriatric endothelial dysfunction is due to an imbalance between reactive oxygen species (ROS) and levels of endogenous protective antioxidants. This age-related increase in oxidative stress reduces the bioactivity of the nitric oxide (NO)/cGMP vasorelaxation, resulting in decreased vascular compliance and ultimately age-related arterial hypertension.

Linking oxidant stress with NO-related endothelial dysfunction is a potentially fruitful concept when applied to geriatric vessels. Superoxide generation impairs NO bioavailability, most likely through inhibition of the NO-synthesizing enzyme, endothelial NO synthase (6, 8). Furthermore, large vessel superoxide generation increases and NO bioavailability decreases with age in Wistar-Kyoto and SHR stroke-prone rats evaluated at 12 mo of age (3). In Payne et al., tempol treatment for 8 mo in SHR rats significantly reversed age-related enhanced vascular contraction and the inhibition of the vascular relaxation produced by the NO/cGMP pathway. If indeed the aging large blood vessel increases the production of ROS leading to oxidative stress, therapies might be targeted to the reduction of the offending agents, thereby restoring NO vasodilation capability and either reducing existing hypertension or preventing its development with aging (1). 

Several points flow from these studies. The source of the oxidative stress needs identification. Multiple enzymatic sources of superoxide and ROS exist, including uncoupled NO synthase. Studies are needed to determine how the oxidative stress is produced and the relationship of this pathophysiological increase to advancing age. Geriatric hypertension needs more com-

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prehensive study to include renal, neural, and hormonal control mechanisms that could contribute to the hypertension. Experiments are needed to determine the impact of oxidative stress in the aging blood vessel on other endothelium-derived factors, such as vasodilating prostaglandins, and endothelium-derived hyperpolarizing factor, as well as vasoconstricting factors.

The study of geriatric hypertension with systolic pressure increase and widened pulse pressure requires appropriate animal models that approximate the aging in humans. Well-designed scientific experiments are critically needed to further the pursuit of targeted therapies for this growing problem in the aging population.

REFERENCES