There is clear evidence that the vessel wall is an aldosterone target tissue, and that aldosterone at physiological levels produces vasoconstriction by genomic and rapid nongenomic actions. Similarly, in clinical studies cited by Duffy et al., patients with primary aldosteronism show impaired flow-mediated dilatation among other indices of endothelial dysfunction; in addition, mineralocorticoid receptor blockade reverses endothelial dysfunction in patients with hypertension or heart failure. In this issue of the journal Duffy et al. explore vasodilator responses to methacholine, nitroprusside, and verapamil over a wide dose range in good-sized cohorts of hypertensive and normotensive subjects, to establish possible correlations with renin-angiotensin-aldosterone status. This is clearly a worthwhile undertaking, although the authors candidly admit they had expected to find elevated renin in hypertensives to be correlated with most marked impairment in vasodilatation and, in fact, found the opposite.

That said, there are several issues of interpretation and analysis that need to be raised. First is the usage “relative aldosterone excess” in the title and throughout the article. No differences between hypertensives and normotensives were segregated into quartiles on the basis of aldosterone levels nor in either group divided into quartiles, with the exception of the highest renin quartile among normotensives: the significantly higher aldosterone-aldosterone status. This is clearly a worthwhile undertaking, although the authors candidly admit they had expected to find elevated renin in hypertensives to be correlated with most marked impairment in vasodilatation and, in fact, found the opposite.

The views in this editorial commentary are not necessarily those of the editors or of the American Heart Association. From Prince Henry’s Institute of Medical Research, Clayton, Victoria, Australia.

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the renin-angiotensin-aldosterone system (eg, sodium deficiency) and exogenous, nonphysiological inputs (eg, angiotensin infusion), in which the normal homeostatic negative feedback mechanisms cannot operate. Much of the conflict is also in a sense artifactual and might be, in part at least, resolved by acknowledging that most mineralocorticoid receptors are occupied by normal circulating levels of glucocorticoids. Under normal conditions, physiological glucocorticoids act as mineralocorticoid receptor agonists, but when the protective enzyme 11β-hydroxysteroid dehydrogenase is blocked or deficient (in epithelia, or the vessel wall), cortisol becomes a mineralocorticoid receptor agonist; the same antagonist-to-agonist change is seen when intracellular redox state is altered by generation of reactive oxygen species. The focus on aldosterone, rather than mineralocorticoid receptor status, is thus less likely to yield unequivocal results than studies using receptor antagonists, which block the effect of whatever agonist. If, on the other hand, the data in Figures 1 and 42 can be validated, the present article may make a much more important contribution than the authors, who set out to prove the opposite, ever dreamed of.

References
Relative Aldosterone Excess: Relative to What?

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