**Contribution of Endothelial Nitric Oxide to Blood Pressure in Humans**

To the Editor:

Assessment and dissection of the various components contributing to the complex regulation of blood pressure control is a challenging task, particularly so in humans. Gamboa et al.¹ are to be complemented on a perceptive and sophisticated study design in their approach to assess the contribution of endothelial-derived NO to blood pressure in humans. Inducing autonomic blockade by infusion of the ganglion blocker trimetaphan to eliminate baroreflex mechanisms, in concert with systemic inhibition of NO synthase, using \( N^\text{G} \)-monomethyl-L-arginine, allowed them to estimate the contribution of endothelium-derived NO to blood pressure in healthy humans, pinning it down to an effect in the magnitude of \( \simeq 30 \) mm Hg. In accordance, the \( N^\text{G} \)-monomethyl-L-arginine–induced increase in blood pressure during autonomic blockade was blunted in smokers assumed to be characterized by impaired NO availability.

In a series of experiments using similar methodologies and systemic NO synthase blockade, we have investigated the role of endothelium-derived NO in another circulatory bed known to be strictly controlled by a variety of components, including the sympathetic nervous system, namely, the renal vasculature. In the absence of autonomic blockade, we could not detect any differences in \( N^\text{G} \)-monomethyl-L-arginine–induced changes in systemic blood pressure or renal plasma flow between healthy control subjects and age-matched patients with hypertension,² diabetes,³ or smokers,⁴ despite proven impairment of endothelium-dependent vasodilation in the forearm in some of these patients. However, common to all of these pathologic conditions was a substantial and significant augmentation of endothelium-dependent increases in renal plasma flow during concomitant infusion of the antioxidant vitamin C, particularly in smokers, thereby highlighting the profound impact of the abundance of reactive oxygen species on circulatory control, at least in the renal vascular bed in these populations. The absence of differences in response to blockade of endothelial NO synthase by \( N^\text{G} \)-monomethyl-L-arginine and the similar blood pressure levels compared with control subjects could be the result of other mechanisms compensating for impaired endothelial NO availability, such as alterations in other endothelium-derived factors or in regulation of sympathetic nervous system activity. Extrapolating these findings to the data presented by Gamboa et al.,¹ one could expect that additional introduction of antioxidant measures in their smokers would have helped to further identify and unmask the contribution of oxidative stress as a cause for the impairment of endothelium-derived NO availability. One aspect that has been neglected in the discussion but certainly needs to be taken into account is the potential influence of activation of the renin–angiotensin system, known to interfere with the sympathetic nervous system, as well as the L-arginin/NO pathway, particularly through nicotinamide-adenine dinucleotide phosphate oxidase-dependent production of oxygen-free radicals, both on a central and peripheral level.⁵

**Disclosures**

None.

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