Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Response

We agree that measurement of forearm blood flow (FBF) is an excellent tool to study vascular pharmacology and physiology in humans and that the vascular effects of aldosterone are not easy to discern because of the complex reactions by different systems. Our main objective was to study interactions between the rapid effects of aldosterone and other vasoactive mediators. We did not use the measurement of FBF of the contralateral arm in this setting. We compared FBF during aldosterone infusion with FBF during placebo infusion, as shown in Figure 1 of our paper. Therefore, the effects in the infused arm cannot be due to changes in the contralateral arm. We know that we cannot exclude systemic effects due to a possible spillover of the intra-arterially infused aldosterone by the placebo control, but such effects are not very likely, as neither blood pressure nor heart rate were affected (Table of our paper). As pointed out by Schmitt et al, the contralateral arm may be preferable as control in certain settings, but for our study design focusing on the interaction between vasoactive substances, we strongly feel that placebo was the appropriate control. In addition, the aldosterone preparation used in our study contained mixed micelles to keep aldosterone in solution, for which we could only control by using a placebo containing mixed micelles without aldosterone. We admit that performing both types of control would have been the optimal solution.

Schmitt et al refer to 2 other studies examining nongenomic aldosterone effects in the human forearm. The first study showed no effect of aldosterone on FBF: aldosterone induced a statistically nonsignificant trend toward an increase of FBF. Using much lower doses, the extent of the increase was about half of the increase seen in our study (4.1±10.3% versus 7.9±2.6%, mean±SE). In our opinion, the lack of nongenomic effects in the study by Gunaruwan et al is mainly due to the higher variability in the FBF measurements and the small number of volunteers (9 versus 48 in our study). Thus, we do not believe that the study by Gunaruwan et al contradicts our results. Both reports are compatible with the notion that the rapid, nongenomic effects of aldosterone are relatively small “low ceiling effectors.” For this reason the results of Romagni et al are quite surprising. In their study a very low dose of aldosterone (resulting in aldosterone concentrations in the forearm within the normal regulatory range) caused a decrease of FBF by about 70%. This huge effect, which would suggest that aldosterone is one of the strongest vasoconstrictors, is rather difficult to explain. The study of Romagni indeed contradicts the results of Gunaruwan et al and our own results.

Finally, we do believe that the major point of our study is the interaction of aldosterone with L-NMMA, NO, and phenylephrine rather than the small vasodilatory effect of the aldosterone infusion itself. We believe that this interaction contributes results from the diverse nongenomic effects of aldosterone, including vasodilation in some vascular beds and vasoconstriction in others that have been previously described and are discussed in our paper. We hope that our study will motivate other groups to join us in characterizing the vascular nongenomic aldosterone effects in humans in more detail.

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Letters to the Editor: Response
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Hypertension. 2004;43:e2; originally published online December 1, 2003;
doi: 10.1161/01.HYP.0000105112.64044.DE

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
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