

## CORRESPONDENCE

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### Isoflurane-induced Coronary Vasodilation

*To the Editor:*—Recently, Hickey *et al.*<sup>1</sup> demonstrated that isoflurane was, as we had shown earlier,<sup>2</sup> a concentration-dependent coronary vasodilator, but that the vasodilator potency of isoflurane was much smaller than we had found.

Hickey *et al.* state that a goal of their study was “to confirm the provocative results of Crystal *et al.*” Their statement is misleading because they chose a different species (swine *vs.* dog) and a different protocol to introduce isoflurane into the coronary circulation than we used. Each of these factors could have contributed to the difference in results. However, it is difficult to imagine how a species difference alone could have accounted for the much attenuated isoflurane-induced coronary vasodilation in the study of Hickey *et al.* A more critical difference between the studies relates to the protocol used to deliver isoflurane into the coronary circulation. Although Hickey *et al.* used, as we had, an extracorporeal system equipped with an oxygenator to selectively expose a coronary artery to isoflurane, they raised isoflurane concentration in the coronary arterial blood gradually, whereas we exposed the coronary circulation abruptly to blood that had been previously equilibrated with isoflurane. Recent findings from Kenny *et al.*<sup>3</sup> and from our laboratory<sup>4</sup> demonstrated that the coronary circulation adapts to the vasodilator effects of isoflurane over time. If this mechanism were operating during the period that isoflurane concentration was rising gradually in the blood, it could explain the blunted coronary vasodilation observed in the steady-state by Hickey *et al.* It is noteworthy that in all of the *in vivo* studies cited by Hickey *et al.* to support their findings (including one from our laboratory<sup>5</sup>), isoflurane concentration in the arterial blood also increased gradually in accordance with its pharmacokinetics in the alveoli and pulmonary capillary bed.

The findings to date suggest that the reduction in coronary vascular tone by isoflurane is not simply a function of its blood concentration but is also dependent on the rapidity with which this blood concen-

tration is achieved and on the duration that the coronary circulation is exposed to isoflurane.

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*In Reply:*—Crystal is correct in his assertion that, if we wanted to exactly duplicate his work, we should have used dogs as our experimental animal and should have selectively perfused a coronary artery with blood already equilibrated with isoflurane as he did in his work.<sup>1</sup> Instead, we conducted our studies in swine, an animal model with a coronary circulation somewhat similar to humans, and we used a membrane oxygenator, which more closely resembles the normal lung with regard to uptake of a volatile anesthetic.

We agree with Crystal and also speculated in our discussion that one of the reasons for the differences in findings between the two studies was the abrupt exposure to isoflurane employed by Crystal *et al.*

It is difficult for us to believe, however, that duration of administration of isoflurane in our study led to a blunted vasodilator response. As stated in our article, we administered isoflurane for 15 min, and coronary blood flow was constant over the last 5 min of this 15-min period. Crystal *et al.*'s work supports our belief that duration of administration did not play a role in our findings, because he reported that at 15 min isoflurane, vasodilation is at a maximum and only begins to decay thereafter.<sup>2</sup>

In summary, Crystal *et al.* exposed coronary arteries to blood pre-equilibrated with isoflurane and found that, under these unique conditions, isoflurane caused a near-maximum vasodilation. This is an important finding that, when explored further, may provide insight