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In Reply:—I thank Professor Jorge Dagnino, M.D., for his chronology of the founding of the Royal Society. With my six-sentence limitation on caption space for *Anesthesiology Reflections*, I thought that I had dealt reasonably with the Royal Society's nebulous origins by writing that Wren, Boyle, and others had met "by" (not "first met") in November of 1660.

Just as I acknowledged 21 yr ago, Wren was the "brains" behind the intravenous goose quill experiment of 1656.[1] So I concur with Professor Dagnino on these facts. In "Boyle, a Most Skeptical Chemist," the 1659 date in the caption was my typographical error.[2]

My thanks to Professor Dagnino for his thoughtful feedback on my telegraphic captions.

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Esmolol May Abolish Volatile Anesthetic-induced Postconditioning by Scavenging Reactive Oxygen Species

To the Editor:—We read with great interest the article recently published by Lange *et al.*[1] In an *in vivo* rabbit model of myocardial ischemia–reperfusion induced by 30 min of coronary occlusion and 180 min reperfusion, the authors observed that β-adrenergic receptor blockade during early reperfusion with either the β1-adrenergic blocker esmolol or the β2-adrenergic blocker ICI 118,551 abolished desflurane-induced postconditioning cardioprotection manifested as reduced myocardial infarct size. However, neither esmolol nor ICI 118,551 had a significant effect on postischemic myocardial infract size when used alone during the first 30 min of early reperfusion, in the absence of desflurane. This is a very interesting finding. However, the more interesting point of the study, as commented on by Dr. Riess in an editorial[2] accompanying this article, is that sustained β1-blockade with esmolol during the entire period of reperfusion not only failed to abolish desflurane-induced postconditioning cardioprotection, but instead actually conferred a similar degree of cardioprotection. We want to join Dr. Riess[2] in congratulating the authors for this comprehensive study detailing the role of β-blockers in volatile anesthetic postconditioning. However, we do not entirely agree that the energy-sparing effect of β-blockade, mainly heart rate reduction, may have been the principal reason for the infarct size reduction. We propose that β-blockers may have conferred cardioprotection primarily by reducing the production of reactive oxygen species (ROS)[3,4] during reperfusion, and that esmolol may have abolished desflurane-induced postconditioning by scavenging ROS.

ROS has been shown to play an essential role in β-adrenergic signaling in cardiac myocytes.[5] Volatile anesthetic-induced generation of small amounts of ROS plays a critical role in anesthetic preconditioning,[6,7] and likely in anesthetic postconditioning as well, since they share similar mechanisms. Esmolol has been shown to increase antioxidant activity and reduce ROS-induced lipid peroxidation in patients with acute myocardial infarction.[8] Therefore, it is reasonable to postulate that esmolol abolished desflurane-induced postconditioning *via* its antioxidant action in the study of Lange *et al.*[1] If this is the case, it could be possible that the cardioprotection conferred by a combination of desflurane postconditioning and delayed β-adrenergic blockade during reperfusion could be superior to desflurane postconditioning or β-adrenergic blockade alone. We are interested in the authors' opinion on this possibility, and the clinical relevance of their findings.

It should be noted that the volatile anesthetic isoflurane-induced ROS production and anesthetic preconditioning cardioprotection is attenuated in senescent hearts,[9] likely because ROS production is already increased in the senescent. Information regarding the age or body weight of the study animal (New Zealand White rabbits) is not provided in the study of Lange *et al.*[1] Presumably, the study was conducted in young animals. It would be also interesting if the authors could provide this information and comment on the potential effect of aging on the effectiveness of anesthetic postconditioning.

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In Reply:—We thank Drs. Xia and Irwin for their interest in our study on the role of β-adrenergic signaling in anesthetic postconditioning[1] and in the accompanying editorial view.[2] We agree with Drs. Xia and Irwin that, besides their energy-sparing effect, several alternative mechanisms of β blockers might be responsible for their infarct size–reducing capacity. Apart from their effect on the interaction between β receptor activation and reactive oxygen species production[3] and scavenging,[4] β blockers can inhibit calcium/calmodulin -dependent protein kinase II[5] and phospholipase A,[6] exert membrane stabilizing effects,[7] and may even have direct effects on mitochondrial electron transport and reactive oxygen species production.[8] The role of alternative mechanisms is certainly supported by the finding that infarct size reduction by β blockade is independent of heart rate, the main determinant of myocardial oxygen consumption.[9] It is entirely conceivable that the combination of different cardioprotective principles at different time points during reperfusion might provide additive protective effects. In this context, it is of interest that calcium/calmodulin -dependent protein kinase II is necessary for desflurane-induced postconditioning, whereas prolonged postischemic calcium/calmodulin -dependent protein kinase II blockade might attenuate adverse effects of ischemia/reperfusion injury, including remodeling.[10] Thus, it might be reasonable to apply anesthetic postconditioning at the onset of reperfusion and to initiate β blockade later during reperfusion. However, further basic research and clinical studies will be necessary to determine an optimized cardioprotective approach and to identify the possible clinical consequences of these experimental findings.

The rabbits used in this study were between 8 and 12 weeks of age and weighed between 2.5 and 3.0 kg. Although cardioprotection by ischemic[11] and pharmacological[12] preconditioning can be attenuated or lost in senescent hearts, there is some evidence of preserved ischemic postconditioning in the aged myocardium.[13] Thus, the impact of aging on the cardioprotective effects of β blockade, anesthetic postconditioning and their interaction with reactive oxygen species needs to be determined in future studies.

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Goals Neither Validated Nor Met in Goal-directed Colloid *versus* Crystalloid Therapy

To the Editor:—Kimberger *et al.*[1] and the editors[2] are to be commended for attempting to shed light on an important topic: What is the optimal intraoperative fluid and resuscitation target?

Many experienced physicians, including us, who provide anesthesia for major intraabdominal surgery have evolved over time from crystalloid-only, "show me the proof" physicians to those being in philosophical agreement with both the author and the editorial writers— goal-directed therapy with colloid is best in intestinal cases. We believe this produces less gut edema without compromising gut or other critical organ perfusion (not to mention reducing the anesthesiologist's aural discomfort from the oft repeated surgeon lament that the anesthesia team is "drowning" the patient). Indeed, Victor Hugo once said, "All the forces in the world are not so powerful as an idea whose time has come."*

Unfortunately, despite our hope to the contrary, all the forces in the world may have to wait a little longer, because this study does not

The above letter was sent to the authors of the referenced Editorial. The authors did not feel that a response was required. —James C. Eisenach, M.D., Editor-in-Chief.

*Available at http://famouspoetsandpoems.com/poets/victor_hugo/quotes. Accessed May 29, 2009.