In Reply:—We thank Dr. Dupanovic for his comments regarding our article, giving us the opportunity to point out some important questions in this field of research.1

First, Dr. Dupanovic states that our results appear surprising, with an intubation success rate of about 50% for the conventional technique with a Macintosh blade and about 90% with the GlideScope (Verathon Medical Europe, Ireland, Netherlands). However, when you compare our results with other studies looking at the success rate of intubation performed by medical personnel intubate only occasionally, or in novices of tracheal intubation, these results are very similar.2,5

Second, according to Mulcaster et al.6 manikin-only training is inadequate for learning tracheal intubation properly, and the step from manikin intubation to intubation of patients makes a major difference. We totally agree. That is exactly the point where difficulties for the inexperienced operators occurred. They had to deal with airways that differed from patient to patient, and they had to overcome their reluctance to use the necessary force to lift the laryngoscope against the resistance of the soft tissue. At this early step of training, the novices felt much more comfortable and had a higher success rate with the GlideScope technique.

Third, Dr. Dupanovic points out that the operators failed to intubate because they failed to achieve a better view of the glottis. Dr. Dupanovic speculates that they might have benefitted from difficult airway training at the manikin before their first intubation attempts in patients. This might have been true. However, we kept our training close to the present training for paramedics, medical students, or novices in anesthesia. Currently, these training sessions start with normal, “easy” intubation in the manikin and patients and progress to difficult intubation after the students have learned easy intubations. In most training centers, manikins for simulated difficult airway training are not available yet. We share the view that training of simulated difficult intubation before intubation of patients might have changed our results, but that was not our study design. We think it is a good idea to integrate simulated difficult airway training in the upcoming years, even for beginners before intubation of patients.

Fourth, the conventional laryngoscope with a Macintosh blade is still the most common approach for tracheal intubation. It is widely available, less expensive, and the maintenance is easier than that of the GlideScope. Therefore, in the near future the GlideScope and comparable devices cannot entirely replace the conventional technique, but can be looked upon as an important alternative technique for expected and unexpected difficult intubations.

Finally, the most important question is whether the extensive use of alternative laryngoscopes lead to a deficit in training and skills with the conventional laryngoscope. Dr. Dupanovic states that in the beginning, training with the GlideScope might improve the training with the Macintosh blade because the trainees recognize what they are supposed to see, and the attending anesthesiologist can give more precise directions.

However, after the first improvements they might not progress to a level that they might reach if they are solely focused on the conventional technique. Basically, this dilemma is comparable to the situation in obstetrics, where the skills for difficult intubations can hardly be taught because most cesarean deliveries are performed under regional anesthesia; therefore, the residents might not get enough exposure and experience.

Overall, we think that for anesthesia residents tracheal intubation with conventional laryngoscopes should still be one of the major skills that have to be learned during residency. It is the obligation of the attending anesthesiologists to ensure that the residents receive enough exposure and expertise under controlled conditions.

In contrast, for medical personnel who only perform occasional intubations, often in emergency situations, it is not the place and the time to train difficult airway management with the conventional laryngoscope but to switch to a monitor-assisted device like the GlideScope that has a higher success rate. A success rate of about 50% in rather inexperienced medical personnel is too low to withhold more effective devices, even when their overall training with the conventional laryngoscope might suffer. Therefore, in the setting of the emergency room or in the field in highly equipped ambulance cars, a device like the GlideScope should be available. Future research will show if significant improvements can be made.

We thank Dr. Dupanovic for voicing his concerns and pointing out how much is still unclear in this field. We also thank the editor for presenting this important discussion.

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Propofol and Cardioprotection against Arrhythmias

To the Editor.—We read with great interest the article by Hirata et al.,1 showing in rats a protective effect against arrhythmias induced by 30 min of left anterior descending coronary artery ligation. The authors suggest that propofol preserves connexin 43 (Cx43) phosphorylation during acute myocardial ischemia, and that this might better protect the heart, as compared with sevoflurane. This effect would be mediated through vagal nerve stimulation. We would suggest another factor that could play a role in the results obtained in this very interesting study.

As Hirata et al. state, chronic heart failure, myocardial infarction, and acute myocardial ischemia reduce the phosphorylation of the

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most important protein of the cardiac gap junctions, Cx43, causing cellular uncoupling and arrhythmias. In a model of myocardial infarction by coronary ligation carried out in both wild-type and inducible nitric oxide synthase (iNOS) knockout mice, Jackson et al. showed that increased nitric oxide production by iNOS has a role in reducing the myocardial content in phosphorylated Cx43 and the ratio of phosphorylated to total Cx43. The mice with iNOS deletion were, as compared with the wild-type mice, relatively protected against reduced Cx43 expression and the consequent depression in cardiac performance.

Propofol has also been shown to down-regulate iNOS expression in macrophages activated by lipopolysaccharide and in a model of tis-ticular ischemia-reperfusion injury in rats.

Furthermore, propofol, as compared with sevoflurane, provides major protection against ischemia reperfusion injury induced by aortic clamping in a piglet model, reducing more the systemic inflammatory response and the expression of nuclear factor-kappa B and iNOS.

It is therefore possible that the stronger depressive effect of propofol on iNOS, as compared with sevoflurane, causes a minor down-regulation of total and phosphorylated Cx43, contributing to the antiarrhythmic effects observed in Hirata et al.’s study.

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In Reply—We are grateful to Dr. Siracusano for the helpful com-
ments regarding our article. As Dr. Siracusano suggests, the effects of propofol on inducible nitric oxide synthase (iNOS) might be another factor of preservation of phosphorylated-connexin 43 contributing to the antiarrhythmic effect.

While we have suggested that propofol reduced ischemia-induced arrhythmias through vagal nerve stimulation, the effect of propofol on nitric oxide production or iNOS have not been mentioned in our manuscript.

It has been reported that propofol has a number of nonanesthetic effects. Regarding nitric oxide, not only does propofol inhibit iNOS, but it also stimulates constitutive nitric oxide production as previously shown by Yamamoto et al. They showed that propofol caused the enhancement of nitric oxide production in cultured rat ventricular myocytes mediated by muscarinic acetylcholine receptors activation. This cholinergic nitric oxide–cyclic guanine monophosphate signaling pathway might be associated with our suggestion that propofol would stimulate the cardiac vagal nerve system.

Regarding the relation between antiarrhythmic effects via vagal nerve stimulation and nitric oxide production, there have been several studies showing that nitric oxide plays an important role. Black et al. demonstrated that nitric oxide mediates the vagal protective effect on ventricular fibrillation, and that those effects were blocked using the NOS inhibitor Nω-nitro-arginine and reversed by replenishing the substrate for nitric oxide production with L-arginine in an isolated rabbit heart. Moreover, Zhang et al. showed that a nitric oxide donor, S-nitroso-N-acetyl-I, 1-penicillamine, partially inhibits the hypoxia-induced reduction of connexin 43 in H9c2 cells, immortalized ventricular myoblasts from rat embryos. This cholinergic nitric oxide-cGMP signaling pathway could be associated with not iNOS, but neural NOS.

Based on these results, further investigation of the effects of propofof on nitric oxide production, iNOS, and neural NOS, which is associated with ischemia-induced arrhythmias, is required.

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