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In Reply:—We agree with Dr. Van Aken that the reports on the cardiovascular system are conflicting, and we agree with all three letters that anesthesia with propofol can be associated with marked reductions in cardiac output, a finding generally supported by much of the literature published since our review was written.

Drs. Merin and Van Aken raise an interesting point when they suggest that in the studies where cardiac output is not affected, there is significant respiratory acidosis. In the study by Claeys *et al.*,[1] although the *p*H fell from 7.38 to 7.30 (mean), the arterial P_{CO_2} increased from 38 mmHg to only 42 mmHg (mean) while the subjects were breathing room air. On the other hand, and as Dr. Merin states, Stephan *et al.*[2] found that hypercarbia resulted in no depression of cardiac output compared with awake controls, while normocarbia and hypocarbia resulted in significant (15%) decreases in cardiac output. While respiratory status is undoubtedly one factor modifying the cardiovascular effects of propofol, other factors such as pre-existing disease state and medications, intravascular volume status, and other anesthetics are also relevant. For example, nitrous oxide is known to cause cardiovascular depression in combination with other anesthetics,[3] although this has been shown not to be an important effect following a single induction dose of propofol.[4]

Most authors agree that propofol has a vasodilating effect and that systemic vascular resistance (SVR) is decreased,[5,6,*] although Van Aken's group found major effects on cardiac output and stroke volume but only minor effects on SVR[7] or an increase in SVR with intubation.[4] Lepage *et al.*[8] also found the reduction in arterial pressure following propofol alone to be related entirely to a decrease in cardiac index and preload, with SVR remaining unchanged. In an open-chested pig model, propofol was found to produce a dose-related decrease in myocardial contractility associated with an increase in SVR.[9] There appears to be no way to reconcile these different findings. Similar anesthetic protocols have been used, generally resulting in a decrease in SVR, yet in a limited number of studies, SVR is unchanged or increased.

Both Van Aken and Lippmann and Mok comment on our statement that "propofol in combination with an opioid may constitute safer practice and offer more effective blunting of autonomic sympathetic responses." This statement related to the study of Stephan *et al.*[6] in which myocardial lactate production was found using propofol alone but when fentanyl was added and surgery was started, myocardial blood flow, arterial pressure, and heart rate returned towards baseline. These results were confounded by surgical stimulation. The recent data of Van Aken *et al.*[7] and Lepage *et al.*[8] suggest that the addition of fentanyl to either a bolus dose or an infusion of propofol results in deleterious cardiovascular effects.

In summary, although the circumstances under which SVR and cardiac output are affected remain to be fully elucidated, a marked decrease in arterial pressure is a universal finding after induction with propofol. The cardiovascular effects of this drug are, as the authors of the three letters point out, more pronounced than those following the usual iv anesthetic agents.

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